

The
Pathology & Therapeutics
of
Acute Rheumatism;

with special reference to the relative
advantages of the different Salicyl
compounds.

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Contents.

| | |
|---|-----------|
| Introduction ; | Page. |
| Definition, Etiology Symptoms & Progress | 4 to 15. |
| Pathology &c. ; | 16 to 39. |
| Treatment ; | 40. |
| Physiological and Therapeutical actions of the Alkalies | 46 to 51. |
| Do. of Salicin & the Salicylates | 52 to 68. |

Cases ; -

| | |
|------------------------------------|-----------|
| <u>I to III</u> (Alkalies) | 70 to 72. |
| <u>IV to IX</u> (Salicin) | 73 to 75. |
| <u>X to XII</u> (Ac. Salicyl.) | 76 to 79. |
| <u>XIII to XV</u> (Potass. Salic.) | 80 to 83. |

Cases (cont.),

XVI to XVIII (Sodae Salic.) 84 to 86

XIX to XXVI —

(to illustrate special
points in Pathology
& Treatment. } 87 to 96.

Results; 97 to 107.

Conclusions; 108 to 112.

Literature; 113 to 123.

Works & Authors quoted; 124 to 125.

4.
Rheumatic fever, or acute articular rheumatism, from its comparative frequency in Great Britain, especially occurring amongst those who are liable to exposure, is of especial interest to the profession at large. Its symptoms, duration and progress have been carefully studied and observed for the last two hundred years, and, despite everything, little advance has really been made in treatment, until the introduction of Salicin by Dr J. I. MacLagan in 1874.

The revolution in methods of medicinal treatment, which were previously innumerable, has led to their total rejection in favour of what now deservedly marks an epoch in the treatment of acute rheumatism.

Previous to the introduction of the alkaloid of the willow bark the alkaline

5
salts of soda and potash were generally employed on account of the more or less generally accepted lactic-acid theory of the pathology of acute rheumatism. Still, expectations were never realised, and, consequently, the explanation of the morbid process doubted.

With a new departure, whose value is now absolutely confirmed after thirteen years experience, some new light has been thrown on the morbid agencies at work; and, though the facts are not yet satisfactorily established, a stimulus has been given to further investigation and elucidation of a most interesting problem of scientific medicine.

6

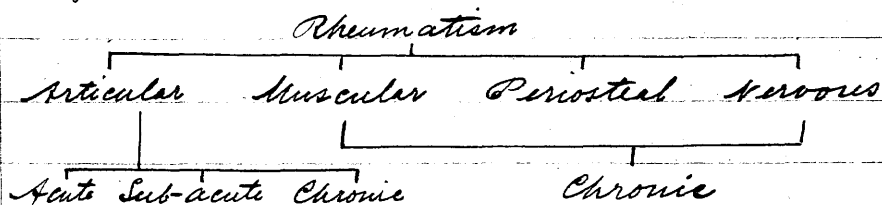
Rheumatism (Latin, Rheumatismus; Greek, Ρευ^{ua}τισμος, from Ρευμα = a watery humour, from Ρεω = to flow), as its derivation proves, was supposed to be a disease caused by a defluxion of the humours of the body, — an idea in accordance with the old humoral theory of pathology.

Acute articular rheumatism, or rheumatic fever, is an acute febrile disease, depending apparently on some general or diathetic influences and characterised by sweats and shifting inflammatory affections of the joints and other fibrous tissues.

Among the ancients, rheumatism seems to have been unrecognised as a separate disease, since no description of the combination of symptoms, known to us as such, can be traced.

Sydenham, in 1670, was the first to describe it and distinguish it from gout, with which it was previously always confounded under the general name of Arthritis.

For convenience in description, rheumatism may be classified in the following manner.



In the Articular form, the joints and fibrous tissues generally are most involved.

In the Muscular form, the tendinous extremities and aponeuroses are the seat of the morbid changes, and not the muscular tissue itself.

In the Periosteal and Nervous or Neuralgic forms, these tissues are respectively the seat of the pathological changes.

8.
Of these varieties of Rheumatism possibly the neuralgic is the one most commonly overlooked; though it not infrequently occurs as sciatica, inflammation of the sclerotic of the eye, spinal meningitis and neuralgia of the mammary gland, uterus and ovaries.

The muscular form is generally seen as lumbago, torticollis, &c.

In the Muscular, Periosteal and Neuralgic forms of Rheumatism there is no fever, and, as they all tend to run a chronic course, they may be classed together. Nevertheless, they may vary within very wide limits as to the severity of the pain (this being the symptom, *par excellence*) in individual cases.

9.
The essential cause of acute rheumatism appears to be chill from exposure to cold and getting wet. Sudden exposure to cold after exercise, wet clothes and damp feet are commonly the precursors of an attack of rheumatism.

That persons may undergo exposure without harm points to a predisposing cause in many; and, again, it is found in practice that the children of rheumatic parents are on the whole more liable to suffer than others. Acute rheumatism is essentially a disease of youth and early manhood, young children being rarely affected and old people suffering generally from the chronic forms of the disease in the joints.

Scarlet fever, gonorrhoea and the parturient state often precede

attacks of acute rheumatism, and seem to have some direct association with the disease, though their pathological identity may be disputed.

Climate seems to have a considerable influence on the rheumatic process; the disease being as a rule more prevalent in cold and damp regions than in warm and dry countries. In the British Isles, the enquiries of the Collective Investigation Committee of the British Medical Association^a found little, if anything, beyond the almost universal prevalence of the disease. Exceptions were found in small towns and villages near the sea coast in Scotland. In England and Wales, three inland spas on elevated sites appear to be free from rheumatism, — Buxton, Old Swindon

^a. British Medical Journal, Vol II, 1889, p 113.

and Laudrimond wells.

A striking feature of rheumatism is the tendency which it has to recur at intervals, on exposure. Yet this may be only apparent, and due, for the greater part, to the diathesis of the individuals. In this respect acute rheumatism differs from the acute specific fevers, of which one attack generally gives immunity to the patient from a recurrence of the disease.

The aetiology of acute rheumatism tends to place it along with such affections as erysipelas, acute nephritis and pneumonia, and the postmortem lesions partake no more of the constitutional nature than any of these affections named. By "local", as distinguished from "constitutional" disease, I take the definition to be, — one involving a special tissue, but which

12.
happens to be largely distributed throughout the body.

The onset of acute rheumatism is generally gradual, the patient complaining of stiffness soreness in the limbs, before the development of pyrexia. Swelling of one joint, with implication of others by metastasis, is the usual primary indication of the nature of the illness. The fever has as a rule reached its height by the second day. The joint affection is a serous effusion, similar to pleurisy or pericarditis, but does not lead to fibrous adhesions, and rarely to suppuration. The pyrexia often bears a distinct relation to the number of joints affected, though this rule is by no means invariable. Hilton Fagge² quotes Graves as to the possibility of the pyrexia occurring without the

² Fagge's Br. of Med. 1888. Vol II p. 812.

joint affection, and mentions a case in which joint complications were absent in the primary attack, but occurred during a relapse. He thus concludes that acute rheumatism is a general disease, with localisations in the joints. Fever, pain and sweating are the most striking symptoms of the disease. The perspiration is often very profuse and of an acrid odour, alkaline to reaction when freshly exuded, but turning acid by decomposition on the surface of the body.

Copious developments of miliaria and sudamina are not uncommon on the skin. I have seen a patient, whose skin was by no means clean, so covered with sudamina, as to resemble very closely a case of small pox.

Erythema, urticaria and purpura

may occur as complications in acute rheumatism, and are undoubtedly related in some way to the disease.

Affections of the heart are the most serious complications of the disease. Pericarditis, endocarditis or both may occur. ^aFaggi^a puts down the proportion of first cases affected in any of these ways at fifty per cent, which is probably very near the mark, although different writers vary considerably in their estimates.

The younger the patient, the greater the liability to cardiac sequelae.^{B.} Pleurisy is the next most frequent complication met with; the percentage of cases so affected being very difficult to determine, since,

^a Faggi's Br. of Med. 2nd Ed. 1888 Vol. II p. 814
^{B.} vide 3rd table in Dr. Church's paper in St. Bart's Hosp. Reports Vol. XXIII p. 273.

if unaccompanied with severe pain, its presence may be easily overlooked. Bronchitis, catarrhal pneumonia, or lobular pneumonia with hepatisation of a portion of a lung may occur.

Peritonitis, iritis, cerebral and spinal meningitis may also be found associated with the rheumatic condition.

Drs Barlow and Warner have described^a rheumatic nodules, usually found in the neighbourhood of joints, but often on bony prominences such as the tibia and acromion.

^a Transactions of the International Congress, 1881, Vol. III p. 116.

Morbid Anatomy
x

Pathology:-

16.
The morbid anatomy of acute rheumatism throws but little light on the nature of the disease. From their inflamed and swollen condition during the course of the disease, the joints appear to be the foci where the disease displays its activity; and, as might be expected, they reveal the most significant post mortem changes.

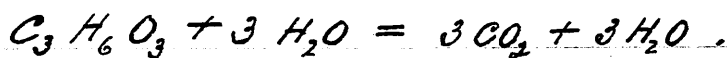
On opening an affected joint, the cavity is usually found full of serous fluid, while the parietal layer of the synovial membrane and the synovial fringes are in a state of hyperaemia. On microscopic examination structural changes can also be detected in the epithelial cells of the synovial surface and in the articular cartilages. The changes rarely pass beyond this stage of inflammation.

7.
Fibrinous clots may be found in the cavities of the heart and large vessels, also evidences of associated pericarditis, endocarditis, pleuritis, meningitis and pneumonia.

The pathology of acute rheumatism has at different times excited a great deal of controversy, and, in spite of the numerous theories advanced (of its causation) from time to time, no perfectly satisfactory explanation of the essential nature of the disease has been established.

The lactic acid, ~~tox~~ nervous, infective, germ and malarial have been the chief theories upon the subject. The lactic acid theory (held by Proutt, Todd and Richardson) supposes the disease to be due to the accumulation in excess of lactic acid in the blood,

and that it acts as a direct poison on the tissues of the body. Pathologists believe lactic acid to be formed in the body by the healthy digestion of starchy substances; the lactic acid being again transformed by oxidation into carbonic acid and water.



The increase of lactic acid in the blood may be due to the effect of a chill in preventing or interfering with the normal tissue metabolism.

Dr. Richardson found evidences of endocarditis and fibrinous deposits on the aortic and mitral valves, after injecting a strong solution of lactic acid into the peritoneum of a cat.

Dr. B. Foster^a recorded two cases of diabetes being treated with lactic acid, in each of which there

^a British Medical Journal 1871.

19.
occurred painful swelling of the joints
resembling acute rheumatism.

Külz² relates a case in which lactic
acid set up pains, similar in
character to those of rheumatism,
in the hip and thigh

Senator upholds the lactic acid
theory, but is of opinion that its
direct action is on the central
nervous system, and that the
disturbed nervous centres react on
the joints. He recognises, moreover,
in the cases of Richardson, Foster
and Külz, only "personal suscept-
ibility". As a matter of fact,
however, lactic acid, though eagerly
sought for, has never been found
in the blood; and, whilst not
doubting that some abnormal acid
or at least irritating product does
exist in the tissues during an
² "Beitrag zur Path. u. Ther. d. Diabetes".

acute rheumatic attack, I cannot believe that a well known substance like lactic acid can exist in the muscular tissue without being discovered.

The nervous theory (held by Seitz and Canstatt) accounts for the symptoms of the disease by supposing that chill of the surface of the body, especially of the joints and skin, caused perturbation in the corresponding parts of the central nervous system. Thus were the pain, fever and trophic changes of the peripheral parts said to arise. According to Fuller the disturbances of the nervous centres cause, by altering the nutritive functions generally, the retention of some acid poison in the body. In the light of modern research and clinical

21.
observation, this appears to me the most probable cause of the majority of cases met with, and will be criticised in detail later on in this paper.

The infective theory was advanced by Heuter. According to it, chills may be due to the entrance of micrococci into the body, and endocarditis result; the joint lesions being considered secondary and embolic, similar to the articular affections in pyaemia. The extreme rarity, however, of suppuration and disorganisation of structures in the joints of patients suffering from acute rheumatism will not bear out the similarity of the two affections, nor give probability to the theory.

The germ theory (advanced by Salisbury) supposed the presence

of a veritable organism in the blood, —
Zymotosis translucens — ; but
 this has not been confirmed.

The malarial theory (advanced by
 MacLagan) is the most recent and
 supposes the disease to be caused by
 the entrance of a miasm from
 without into the blood. This
 miasm is said to be of the nature
 of, but specifically distinct from
 the poison of malarial fever.
 The theory, though open to many
 objections, has brought about
 the most important results in
 the treatment of acute rheumatism.

In considering the various views as to
 the essential nature of acute rheumatism,
 there can be little doubt that, whatever
 part disturbances of the nervous centres
 may play in the production of the

disease, the proximate cause is the presence of some virus circulating in the fluid media of the body. The next question that presents itself is, - what is the nature of the virus; is it chemical or particulate?

At present this may only be inferred by analogy, as the virus has not yet been ~~scientifically~~ demonstrated by isolation. Local inflammations due to cold or cognate conditions resemble, in their method of production, acute rheumatism in so many respects that they may be meanwhile classed with it as regards their proximate cause. Among these may be mentioned acute bronchitis, pneumonia, erysipelas, nephritis &c.

Since the investigations of Pasteur and Koch into the causation of disease the germ theory has received such

27

an impetus that there is great danger of all other causes, which may produce pathological changes, being overlooked or held in too little esteem. Undoubtedly, however, the germ theory has marked an important era in the history of scientific medicine, and established as facts many ideas formerly theories. The germ theory assumes that all infective diseases are caused by the development in the body of micro-organisms which are introduced from without. Such germs are supposed to be capable of indefinite multiplication within the body when they are introduced in even the smallest quantities. The proof of this position lies in the capability of the pathologist to isolate the organism, cultivate it pure in a nutritive medium, and,

by introducing it into a healthy body, produce the same symptoms again and again.

Different micro-organisms producing different effects points to a kind of selective affinity for tissue or organ, — an idea which must for the present be conceded in following up the subject.

The micro-organisms are of a vegetable nature and classed under the fungi. They are found in abundance in the soil, water and air, and are probably at all times present in great quantities in the animal body. Most of these bacteria are incapable of development in the body: being most likely killed by the vitality of the tissues. Under ordinary circumstances there seems to be an antagonism between the living cellular elements of the bodily tissues

and these micro-organisms, resulting in the triumph of the protoplasmic cells, — a "survival of the fittest." But some are able under favourable circumstances to develop and assume their superiority, with the result of producing pathological changes in the tissues; these again evoking a series of symptoms known and recognised as a specific disorder in the domain of clinical medicine.

Acute rheumatism is one of the few diseases whose pathology has not yet been generally disassociated from the period when all morbid processes were held to be disturbances of the humours of the body. In modern phraseology this means a perturbation into abnormal channels of the normal or physiological changes undergone in

the chemistry of the tissues of the body. Gout and rheumatism were long confused both clinically and pathologically, and even now we may well enquire as to the probability of their being due to analogous causes. The researches of Garrod have left no doubt about the presence of urate of soda in the blood being the toxic agent in the phenomena of acute gout. In each disease hereditary predisposition is well marked, and the following peculiarities are common;—

- (a). Acute febrile disease;
- (b). Localisation of virus in joints;
- (c). Tendency to recur;
- (d). Complications of heart & lungs.

Though these conditions vary somewhat yet they are sufficiently constant and characteristic to establish a clinical relationship between the

28.
diseases, and a strong probability of their proximate causes being similar. Thus I hold it proved that the immediate cause of the rheumatic symptoms is the presence in the blood of some abnormal product (chemical composition as yet unknown) of retrograde tissue-metamorphoses acting as a direct irritant on the serous and white fibrous structures of the body.

That the nervous system plays a by no means inconsiderable part in the phenomena of acute rheumatism, the etiology of the disease will bear out. Its exact nature is uncertain, and cannot be freed from the speculative theories of cerebral functions skilfully built up as a result of physiological experiment.

29
Perhaps the most complete exposition of the associated nervous phenomena is that of Dr. P. W. Latham², as follows.

- "(1) A nervous centre exists which controls the nutrition of the muscular and other tissues, and which has been called the inhibitory chemical centre.
- "(2) The action of cold, on some individuals, by lowering the power of this centre, modifies the nutrition of the tissues, and leads to the excessive formation of lactic acid and other products.
- "(3) The presence of lactic acid in abnormal amount in the blood produces functional changes in the medulla oblongata and spinal cord (? posterior columns) when brought into contact with them, and develops the local symptoms of acute rheumatism, in a manner similar to the production of the symptoms of locomotor ataxy, with its anarthropathies

a. British Medical Journal, Jan'y 1882.

30
"by organic change.

"(44) In the portion of the medulla
"oblongata in the neighbourhood of the
"origin of the vagus is a point of minimum
"energy, either hereditary or acquired,
"then, according to the particular fibres
"involved, may cardiac, pulmonary
"or pleuritic complications be developed
"during an attack of acute rheumatism."

Most probably the co-ordinating
nervous centres are disturbed, by the
exposure of the surface of the body to
chill; the cutaneous afferent nerves
transmitting the shock to the central
nervous system. The result of this
is to alter in a pathological sense the
metabolism in the tissues of the body,
while the products act more or less as
foreign matter in the physical economy
and give rise to a series of changes
which appeal to the physician as the

signs of disease. But one must take into consideration the association of functions of the different secreting organs of the body (notably, the skin and kidneys), and the fact that pathological changes can be reflected from an exposed organ to one sympathetically related to it in function. This is well exemplified in the case of patients, during the desquamative stage of scarlet fever, after exposure to cold, contracting renal congestion and inflammation. After chill the functions of the skin are interfered with and the elimination of the products, which that organ has to remove from the blood, has to be carried on by some other channel. These poisonous matters, being retained in the blood, may act as irritants to the kidneys, lungs and heart.

Dr. P. Hood* quoting Dr. Bence Jones on the subject of tubular nephritis refers to the excretory functions of the skin and kidneys, and the deleterious consequences of cold in interfering with their physiological actions. He adds; - "the substances, or their parents, that the cortical structures should secrete are left behind in the blood, and from it they pass with the lymph into the structures, according to their powers of diffusion". It has been demonstrated^a that acute rheumatism, following scarlet fever, usually appears during the desquamative stage. Here we have the skin in a condition very liable to be injuriously affected by exposure, and, independently of the renal complication per se, we have a proof of the part played by the

^a See papers by Dr. Barlow and Ashby, in the British Medical Journal, 15th Sept. 1883.

* "Etiol. & Rheumatism" by Dr. P. Hood, 3rd Ed. 1885.

nervous system in the production of an attack of acute rheumatism.

The malarial theory of the causation of acute rheumatism was propounded by Dr. MacLagan and discussed in extenso.² Whilst admitting most of the explanations of the lactic acid theory to be probable, he maintains that the disease is due to a kind of malaria. He believes that "acute rheumatism is accompanied by excess of lactic acid in the system, and such excess is only noted ^{in connection} with it", but denies that there is any "proof that the acid causes the rheumatism". He treats of the nature of malaria and the mode of its action, and gives five points of resemblance between it and the rheumatic process: -

a. Rheumatism, by J. I. MacLagan M.D., 1881.

- (1) The occurrence of the fever.
- (2) The non-elimination of the poison,
- (3) The non-communicability of the disease,
- (4) The varying course and indefinite duration,
- (5) The liability to repeated attacks.

Unfortunately for this theory, the natural history of the disease does not bear it out. The exciting cause is undoubtedly chill from exposure to cold, other conditions being favourable to the production of the rheumatic process. Again, the liability to the disease is confined much more to persons than to districts. The disease, moreover, has been over and over again proved to be hereditary. Regarding "the non-elimination of the poison", and "the non-communicability of the disease" it may be said that they prove no more than a resemblance.

between acute rheumatism and pleurisy or nephritis, - diseases preceded by almost identical conditions.

But the greatest objection to the acceptance of this theory is the fact that, as far as Great Britain is concerned, acute rheumatism is almost universally distributed over the whole country; locality having no apparent influence on its effect or production. Again, - this country is not at all suitable for the production of malaria; and even the districts, where ague used to exist, are proved to be no more liable to rheumatism than others.

It now remains to discuss what part, if any, micro-organisms play in the phenomena of acute rheumatism. That a catarrh, caused by chill,

may be due to the entrance of specific bacteria into the body, in whose tissues they evolve their life history, is quite probable. But, it is just as likely that the presence of micro-organisms in the blood, in such a case, is due to the pathological products of tissue-change affording favourable conditions for their development. The aetiology of acute rheumatism, considered from a bacterial point of view, was discussed by Dr. A. Mantle². Reasoning by analogy, and the results of microscopic examination of the blood of patients, he believed in a specific bacterium producing pneumonia and acute rheumatism. He found, as might be expected, numerous micrococci and bacteria, but nothing of a specific character. The proof can only be obtained by isolating the micro-organisms,

² British Medical Journal; vol. I, 1887, p 1581.

cultivating pure outside the body, and innoculating healthy animals therewith. If the disease be due to the introduction of the micro-organism into the body, the animals innoculated with the pure cultivation will exhibit symptoms similar to the original disease.

In the case of acute pneumonism, no such specific organism has been detected, and, from our knowledge of the disease (especially when compared with those affections known to be of bacterial origin), I believe that such a discovery is extremely improbable. It is but fair to add that Dr. Mantle believed the symptoms of the disease were caused by the chemical products, and not by the action of the micro-organism directly. He also thought it probable that

Lactic acid might be the ptomaine of the disease.

I think it beyond question, however, that, in the products of unhealthy action, micro-organisms, which are known to swarm in all the tissues of the healthy body, may find a nidus suitable for their growth and development. Thus, probably, many of the sequelae of acute rheumatism arise; - e.g. ulcerative endocarditis, from the deposition of micrococci on the cardiac endothelial membrane; chorea, from emboli of micro-organisms; suppurative arthritis, in the joints of strumous subjects; &c.

Now, to briefly summarise, I have endeavoured to prove that, -

(I) the nervous disturbances are the primary factors in the pathology of acute rheumatism, as directly causing the perturbation in the tissue metabolism which results in the formation of abnormal products;

(II) the virus itself is essentially chemical, and produces the usual symptoms of the disease;

(III) conditions, favourable to the development of micro-organisms, occur, giving rise to numerous interesting complications and sequelae.

Treatment, speaking generally, is divided into three parts, — hygienic, prophylactic, and remedial, into the last of which I propose only to enter.

Remedial treatment acknowledges the presence of actual disease, and consists in the cure (or care) of the morbid condition. This can sometimes be accomplished directly by drugs, as in the administration of anthelmintics for *taenia*, &c. Drugs, however, must always take a very low place in the cure of disease, since, in its essence, disease is to be looked on as disordered function, — an aberration from the normal or physiological functions of the bodily economy.

The *vis medicatrix naturae* is our chief therapeutic agency, while, at

the same time, too much must not be left to natural causes. By maintaining the patient's strength, relieving distressing symptoms, guarding against complications, and hastening convalescence (or postponing a fatal issue) the physician has often to be satisfied.

Careful feeding and nursing now deservedly occupy a very high place in the cure of disease, so much so, that, in many cases, little else is required in the treatment of the patient. Free action of the skin, lungs, kidneys and alimentary canal ought always to be looked after to assist in the removal of effete matters from the blood.

In looking over the immense number of measures and drugs advocated at different times for acute rheumatism, one is very much inclined to be sceptical of any new remedy.

Bleeding, blistering, purgatives, diaphoretics, sedatives, mercury, cinchona, colchicum, antimony, aconite, guaiacum, nitre, actea racemosa, lemon-juice, sulphur, potash salts, quinine, veratria and perchloride of iron have all been lauded at different times.

The tendency, of publishing immature results and on wholly insufficient grounds, is much to be blamed.

Apparent successes are often eagerly seized on, while failures are not infrequently ignored. In the midst of so many conflicting statements, the truth is difficult

to find. Regarding this Dr. Sinclair very wisely remarks², — "it is probable that there are cases which yield to every kind of treatment, or to no treatment, and some which pursue their destructive career in spite of all the artillery ⁱⁿ of the pharmacopœia and out of it".

The different theories of the causation of acute rheumatism have all something more or less captivating in them; and, according as evidence in favour of one or other seemed to gain ground, the medicinal treatment was modified or altered.

In trying to alleviate the leading symptoms, — fever, pain and perspiration — we get a general indication for treatment.

The sour-smelling perspiration, so characteristic of acute rheumatism,

a. The Lancet, Feb^y 1880.

has been looked upon as an effort of nature to rid the body of the virus of the disease; and, the idea that this was lactic acid gave rise to the treatment of the disease by alkaline salts, with a view to neutralize the acid poison. Although the identity of the chemical virus has never been proved, the alkaline treatment has long been employed with beneficial results. The joint affections were usually so troublesome as to necessitate the use of local applications in addition.

Salicin and the salicylates have altered this, inasmuch as they give relief to all the symptoms at a very early stage.

In order to establish the relative values of these drugs, I beg to

submit the results of my investigations. The cases were taken as they occurred and treated ; -

- 1st series by Alkalies ,
- 2nd " " Salicin ,
- 3rd " " Salicylic Acid ,
- 4th " " Salicylate of Potash ,
- 5th " " Salicylate of Soda .

These substances all show characteristic differences in therapeutic action , and vary little in their individual actions when unadulterated . Nevertheless , idiosyncrasies occur and complications , in the disease , over which they may be not only inert but prejudicial .

The different combinations of soda and potash form a group of salts possessing a high power of diffusibility; the potash salts in even a greater degree than the soda compounds. In chemical reaction they are all either alkaline or neutral, the degree of alkalinity varying within wide limits. In their affinity for water, the carbonates and bicarbonates come after the caustic alkalis, and possess in a less degree their properties of dissolving the nitrogenous elements of the tissues. By virtue of their diffusibility, the alkaline salts pass readily into the blood, where they undergo various changes according to their composition. Thus the alkalinity of the blood must be to some extent increased, though the salts are rapidly eliminated by the kidneys. Owing to the

47

well-known oxidising action of the alkalis, it may be inferred that the oxidation of the blood and the tissues generally is increased.

Ringer states^a that large doses of potash salts considerably depress the temperature. It is questionable whether these salts act as diuretics on the healthy body, although their diuretic action is easily proved in certain morbid conditions. The acetate and bicarbonate especially are remarkable in this way.

Their mode of action is possibly due to the oxidation of effete matters in the blood, resulting in the formation of urea which is known to have diuretic properties.

In conclusion let me add some quotations from Dr. Ringer^b regarding the action of soda and potash salts.

a. Handbook of Therapeutics by S. Ringer M.D. p 197.

b. *ibid* (10th Ed. 1883) p 200 - 202.

I. Potash salts are all far more poisonous than soda salts.

II. Soda salts, in twice or three times the quantity which proves fatal in the case of potash salts, produce no effects on the system except a passing weakness.

III. The acid of the salt plays no part in the fatal result.

IV. Large doses of potash salts lessen the frequency of the heart's beats, and sometimes make them irregular.^a

V. Potash salts are depressors and paralyzers of the heart, acting, as they paralyze the other structures, by their affinity for the nitrogenous tissues.

The more highly endowed ganglia are the first to suffer; hence small doses will arrest the heart, whilst

a. I have frequently observed large doses of the salts of potash produce irregularity of the cardiac action, both in force and rhythm. A.S.

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V. Potash salts are depressors and paralyzers of the heart, acting, as they paralyze the other structures, by their affinity for the nitrogenous tissues.

The more highly endowed ganglia are the first to suffer; hence small doses will arrest the heart, whilst

a. I have frequently observed large doses of the salts of potash produce irregularity of the cardiac action, both in force and rhythm. A.S.

the muscular tissue will still respond to galvanic stimulation.

Guttman, as quoted by Ringer, found that the injection of small doses into the jugular vein of warm-blooded animals paralyzes through the nervous system; whilst Traube found that the injection of a large dose also acted on the muscular tissue so that it failed to contract on the application of galvanism.

The therapeutic action of the potash salts in acute rheumatism has never been established on a scientific basis.

The lactic acid theory led to their being administered with the idea of neutralizing the poison, but the results have not come up to expectations.

That they have beneficial action in

some cases, even after the failure of salicylates, is beyond doubt. ^a. Their action in reducing the fever and joint pain is, when not assisted by perfect rest, comparatively slight. This may be seen, in the occurrence of exacerbations of the fever and pain, when the patient is allowed to get up and walk about too soon. They undoubtedly assist in the removal of nitrofenous products from the blood, by acting first as oxidising agents and secondarily as diuretics. Thus the temperature is lowered and the joint irritation lessened. I doubt if their direct action on the nerve centres could be pushed sufficiently in the interests of the patient, owing to their depressing action on the heart. Yet in this way, in

^a. See Case XXII p. 91.

moderate doses, they may assist somewhat in reducing the fever.

The employment of Salicin and the Salicylates has altogether proved so satisfactory in the treatment of acute rheumatism, that all other medicinal remedies, at least for routine treatment, are at a discount.

True, the salicyl compounds are not invariably successful, and must not be allowed to some of the older remedies used, - notably the salts of potash.

That Salicin is not even a recent addition to the student of the healing art is proved by the following passage from "Gervard's Herbal."

"The barke hath vertues; Dioscorides writeth, that this being burnt to

"ashes, and steeped in vinegar, takes
 "away cornes and other like risings in
 "the feet and toes; divers, saith Galen,
 "doe slit the brake whilst the Withy is
 "is flouring, and gather a certain juice
 "with which they use to take away
 "things that hinder the sight, and this
 "is when they are constrained to use a
 "cleansing medicine of thin and subtile
 "parts".

In 1830 Leroux obtained salicin from
 willow bark, and from it in 1838
 Piria first isolated salicylic acid.

In 1844 Cahours separated the
 acid from oil of spiraea and winter
 green. Its medicinal properties were
 investigated by Bertagnine in 1855.

In 1860 Kolbe and Lautemann
 made salicylic acid in the laboratory,
 and this was found to be identical
 with that formed by the plant.

Its relation to carbonic acid had been previously pointed out by Stolbe, but in 1874 he discovered how to obtain the one from the other.

Salicin given to healthy individuals must, to produce physiological symptoms, be administered in one large dose, or in several smaller doses repeated at short intervals. Given in small doses, no symptoms appear, as toleration is soon established, when even large doses produce no effects.

Ringer^a describes the symptoms of a person under full medicinal doses in a manner which bears a strong resemblance to cinchonism.

"The expression is dull and heavy, the face quickly flushes on slight excitement, and the eyes become suffused.

"The flush, of rather a dusky hue,

a. Haman's *Therapeutics*, 10th Ed., p. 508.

"suffuses itself uniformly over the
 "whole face. The patient, made more
 "or less deaf, complains of noises in
 "the ears. He complains too of frontal
 "headache, and his hands, when held
 "out tremble a little. His breathing
 "is rather quickened and deepened.
 "Not unfrequently, especially after
 "large doses, nausea and vomiting
 "ensue. In some cases one symptom
 "may predominate; thus deafness may
 "be almost complete, without headache
 "or muscular ~~twitchings~~; or the
 "breathing may be characteristic, and
 "the limbs may tremble, without
 "headache or deafness; but it rarely
 "if ever, happens that any symptom
 "is unaccompanied with the dull,
 "heavy aspect, and the readiness to
 "flush".
 Intense headache, great muscular

irritability, spasmodic twitchings of the limbs and tingling of the extremities sometimes occur. The respiration, pulse and vision may even be impaired.

Salicylic acid and its salts lower the blood pressure, and produce in healthy individuals almost the same physiological symptoms as the alkaloid. In the case of salicylic acid, Dr. Tuckwell observed delirium like delirium tremens, involuntary evacuation of urine and faeces, slow laboured pulse, and olive-green urine.

Probably the alarming symptoms were due to a trace of carbolic acid being in the specimen of salicylic acid used. Dr. Murchison attributes to its effects on the urine the delirium which sometimes follows the use of the acid. Perspiration and

urticarial eruptions, though often seen when the salicylates are given in acute rheumatism, have never been observed when the substances are given to healthy individuals.

Dr. Ringer^a records a series of observations, in carefully drawn up tables, on the action of salicylic acid and salicin on the temperature in health. He shows that large doses of salicin had no appreciable effect on the temperature, and that the only effects apparent were slight deafness and quickening of the pulse. With salicylic acid, even to the extent of 160 grs in one day, he failed to obtain a reduction of the normal temperature of the body. Yet, Dr. Riess got, in 4 to 6 hrs., a constant reduction of 1°F .

^a Handbook of Therapeutics, 10th Ed. p. 601 & 605.

Mr. W. North^a, in the course of some careful experiments on the elimination of nitrogen, was induced to observe the temperature of the urine and the effect of salicylic acid on the temperature of the body. He gives long tables accurately compiled from numerous observations, and arrives at the following conclusions:—

"I. That the temp^r of the urine is "probably always higher than that of "the mouth:

"II. That whilst exercise raises the temp^r "both of the mouth and the urine, "the latter is much more readily affected "than the former, and perhaps in a "greater degree.

"III. That salicylic acid affects both "temperatures, but the mouth more "than the urine, rather preventing a "rise than causing a fall.

a. The "Practitioner", 1879, Vol. XXIII p. 184.

"IV. That whatever be the causes of the ordinary daily variations of temp^r., they affect the urine as well as the mouth."

Salicin requires to be given in much larger doses than the acid or its salts to produce characteristic symptoms.

In my experience the quantities which will produce similar results

are, -
$$\left. \begin{array}{l} \text{Salicin} = \frac{1}{5} \\ \text{Ac. Salicylic} = \frac{1}{5} \\ \text{Sodae Salicylas} = \frac{1}{4} \end{array} \right\}.$$

With regard to the chemistry of their action, Senator first pointed out that the ferments split up salicin into saligerine and glucose, the former being readily oxidised. It is believed that similar changes occur in the blood, though only partially, as salicin can be detected pure in the blood.

Dr. Macdagan^a, in his early observations on the action of salicin and salicylic acid, refused to look upon these substances as antipyretics to any useful extent, inasmuch as, in other febrile diseases than acute rheumatism, they were not nearly so useful in reducing high temperatures as some of the older antipyretics in use. Their action in acute rheumatism was so marked that two questions naturally arose, - (1) as to the pathology of acute rheumatism, and (2) as to the therapeutic action of salicin and salicylic acid.

In attempting to answer the first of these questions, the tonic and antipyretic properties of the alkaloid probably helped to lead Dr. Macdagan astray. Its resemblance in physiological action to quinine was

a. Lancet, 21st June 1879.

notable; and, its therapeutic action in acute rheumatism so much resembled that of quinine in ague, that the idea was easily formed of a similarity in the cause of the two diseases. Everything else, however, points in a different direction.

Senator^a attempted to explain the action of salicine by stating that in the blood it became converted into salicylic acid, which was the true therapeutic agent. The result was that salicylic acid came into use generally for acute rheumatism. The action of the acid was found to be different in some points from that of the alkaloid; and, in order to meet the results of investigation, Senator attempted further to explain the difference as existing between the action of

a. Centrblatt 1876. 4

Berlin Klin. Wochenschrift, 1877.

nascent salicylic acid formed in the blood, and the same substance taken by the mouth.

Salicin given in large doses relieves the symptoms of acute rheumatism in a few days. Small doses are of no avail, and Dr. MacLagan's plan of quickly "saturating the system" generally gives relief within 48 hrs. The physiological symptoms are produced in a slight degree, but sickness and delirium are remarkable by their absence.

Salicylic acid often gives speedy relief in acute rheumatism, but, whilst doing so, often gives rise to troublesome symptoms. I have found the acid produce sickness, profuse perspiration with miliaria, burning sensations

in the throat and stomach, sometimes diarrhoea, and as a consequence great depression. Many of these disagreeable symptoms are prevented if care be taken to use a perfectly pure specimen of the acid, which is usually contaminated with carbonic acid. In acute rheumatism, salicin is much to be preferred to salicylic acid.

Salicylate of potash is in my experience, in acute rheumatism, superior to the acid but inferior to salicin. It almost invariably ^{causes} cardiac depression, as evidenced by irregularity in the force and rhythm of the heart's action.

Profuse perspiration I have often noticed during its administration, and delirium and sickness occasionally.

Salicylate of soda is in my opinion greatly superior to both salicylic acid and salicylate of potash.

It rarely produces any unpleasant symptoms if given in small frequently repeated doses, from the commencement of the rheumatic attack, and then continued thrice daily for 10 or 15 days after the reduction of the temperature to normal. In 15 and 20 gr. doses I have seen it produce headache and noises in the ears, when, in smaller doses (10 grs.), it gave as much relief to the symptoms without the disagreeable effects. In only one instance have I found it cause headache and slight delirium in small doses. It was stopped and alkalis

given, when the patient made a rapid recovery.

As compared with salicin I think salicylate of soda is scarcely inferior in therapeutic value, so long as the cardiac action is good and the patient possesses no idiosyncrasies. And, on account of the comparative smallness of the dose, and its solubility in water, the soda salt is on the whole to be preferred to the alkaloid.

Although all these substances are useful, with the differences noted above, in the treatment of acute rheumatism, none of them will altogether prevent cardiac complications arising during treatment or even subsequently. But, by lessening

the duration of the disease (at least of the acute symptoms), they probably tend to make these troublesome sequelae less common.

Relapses, in my experience, are no more common in cases treated by salicylates than by the old alkaline routine: granted that proper precautions are taken to prevent the patient, who may feel quite well, changing his diet and walking about too soon.

In an article on Febrifuges, Prof. Binz^a of Bonn discussed the action of Salicylic acid. He considers that an important factor affecting the mode of action of the salicylates has been too long overlooked.

"Our tissues", he adds "as is known" continually produce carbonic acid

^a Practitioner, 1876. Vol XVI p 440.

"of which the blood, notwithstanding
 "its alkaliescence, holds a good part
 "in solution, either in a free state
 "or in combinations, from which the
 "carbonic acid is constantly ready to
 "separate. Now this gas developed
 "absolutely pure, possesses the power
 "of setting free the salicylic acid
 "contained in the salicylate of soda".
 The action of salicylic acid as an
 antipyretic was investigated and
 reported by Dr. C. A. Ewald.

He states² that as far as direct
 action is concerned the acid and its
 salts are similar, but recommends
 the soda salt at once, as in all
 probability the acid is "converted"
 "in the blood into the sodium salt".

Mr. Alex. Haig³ has attempted to show
 that within limits it is possible to

a. Practitioner, 1876, Vol. XV. p. 200.

B. Journal of Physiology, Jan'y 1877.

increase or diminish the excretion of uric acid at pleasure, by means of acids and alkalis; that acids always diminish and alkalis increase the excretion. And further, he has shown that headaches due to this excessive excretion of uric acid may be cured and the excess of uric acid secreted may be stopped by the administration of acids.

The same writer points out^a that salicylic acid forms an important exception to the above statement, for, while it increases urinary acidity, it does not in any way diminish the excretion of uric acid. He holds that this action of the salicyl compounds is of great importance in explaining the value of these drugs in rheumatism, gout and other diseases connected

^a Lancet, Jan'y 1878.

with uric acid. Illustrations are given. Excessive excretion of uric acid taking place under salicylates is not accompanied by any headache, and salicylates have been previously found useful by him in headaches due to this cause. The action of acids and alkalis on the uric acid excretion is probably due to the fact that alkalis increase and acids diminish its solubility; salicylic acid being the exception.

Salicylic acid is supposed to be transformed into salicyluric acid, which differs from uric acid in being much more soluble in water and probably also more soluble in dilute acids.

Cases.

Summary of 26 Cases to illustrate comparative Treatment.

Cases 1, 2 & 3 ; - Alkalies.

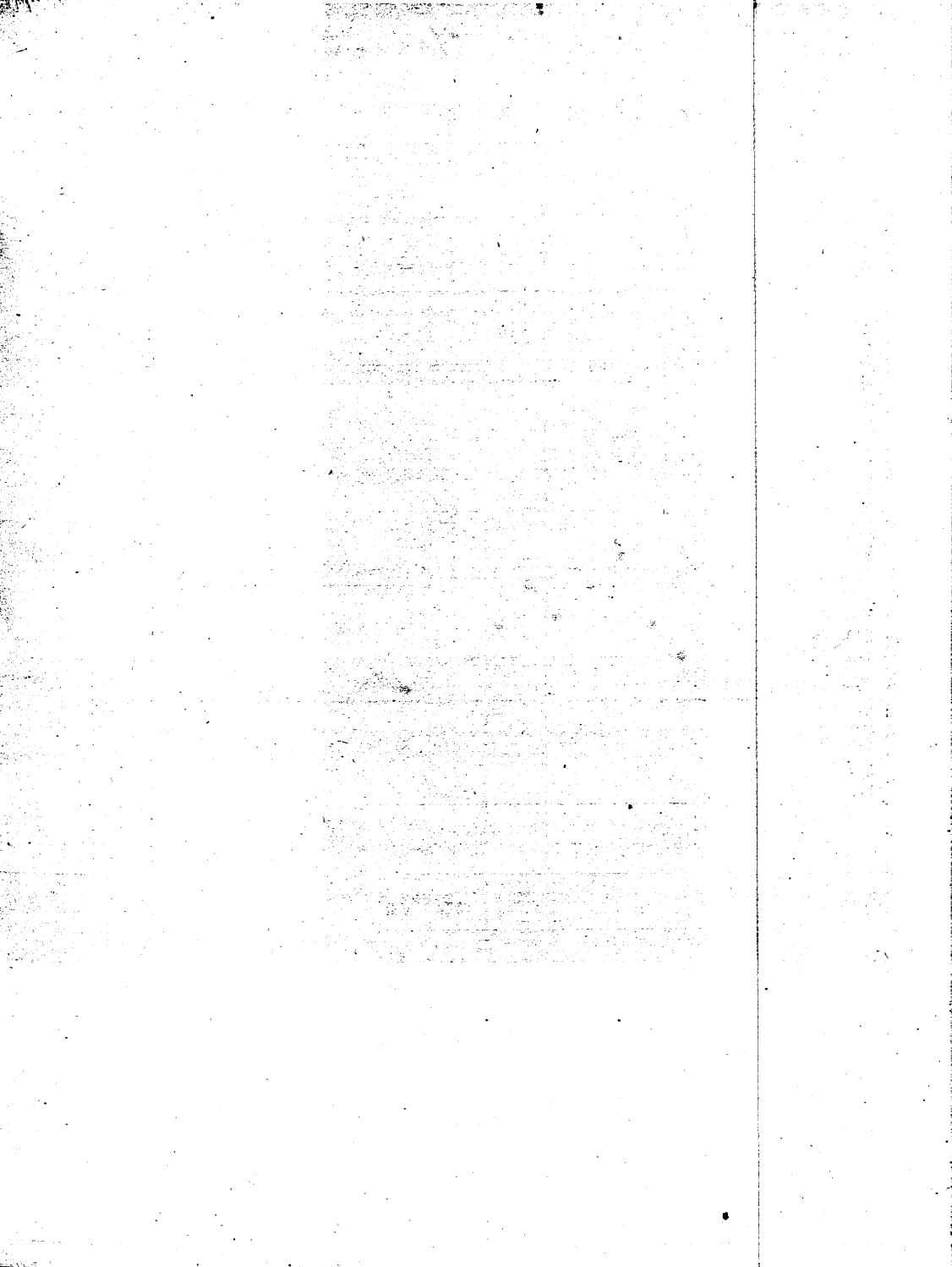
" 4, 5, ~~6, 7~~ 8 & 9 ; - Salicin.

" 10, 11 & 12 ; - Ac. Salicylic.

" 13, 14 & 15 ; - Potass. Salicyl.

" 16, 17 & 18 ; - Sodae " .

" 19, 20, 21, 22, 23, 24, 25 & 26 ; - to illustrate points, in treatment, which have a bearing on the Pathology of the disease.



Name

Joanna A.

Age

16

Disease

Ac. Rheumatism

Result

Cured.

1884
Jan.

25 26 27 28 29 30 31 Feb 1 2 3 4 5 6 7 8 9

TEMPERATURE FAHRENHEIT'S SCALE.

106°
105°
104°
103°
102°
101°
100°
99°
98°
97°
96°

TEMPERATURE CENTIGRADE SCALE.

41°
40°
39°
38°
37°
36°Pulse M
E

102

105

100

102

95

Pulse M

Resp. M
E

40

40

35

30

30

Resp. M

Motions

/

2

/

/

/

2

/

/

2

/

/

Motions

Urine, ozs.

Urine, ozs.

Sp. Gr.

1033

1020

Sp. Gr.

Reaction

Ac.

Ac.

Reaction

Chlorides

Defi.

Nor.

Chlorides

Albumen

Nae

Nae

Albumen

Day of Dis.

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

Day of Dis.

Case I. Joanna A. aet. 16.
 Ad. 29th Jan. 1884.

Complaining of pain in knees and joints of fingers; headache; loss of appetite.

Skin moist; temp^r 102°F; pulse 102, full and bounding; respir^{ns} 40.

Fluid present in knees, esp. the L.

Systolic murmur in mitral area; and a few moist crepitant rales at the apices of both lungs.

Urine, Sp. Gr. 1033, scanty, trace of albumen, and loaded with urates.

History of exposure to wet and chill.

Treatment: - rest in bed between blankets; milk diet; iodide and bicarbonate of potash administered in large doses; joints treated with belladonna liniment and cotton wool.

Fairly convalescent on 9th Feb.; - pulse temp^r and respirations normal. Slight stiffness in knees remaining, with mitral systolic murmur, slight cardiac depression and anaemia.

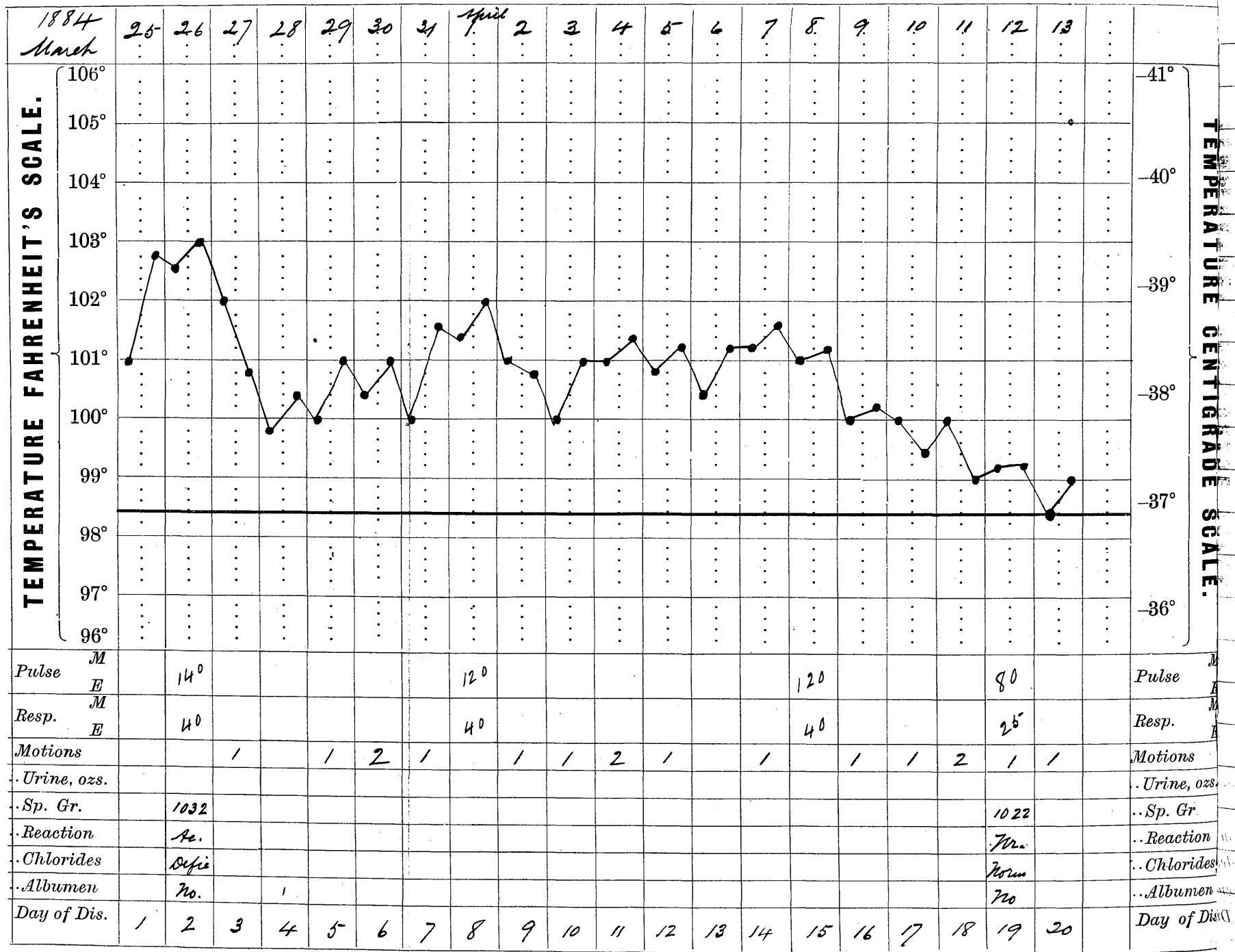
Name Charles M.

Age 28

Disease *Acute Rheumatism* Result *Cured.*

Result

Leind.



71.
Case II. Charles M. act 28.

Ad. 25th March 1884.

Complaining of pain and swelling of the
L. Knee and ankle. Skin moist;
temp: $101^{\circ}7$; respr^{no} 40

The cardiac sounds are feeble but
otherwise reveal nothing abnormal.
Tongue furred and bowels constipated.
Lungs normal. Urine scanty and
depositing urates on cooling.

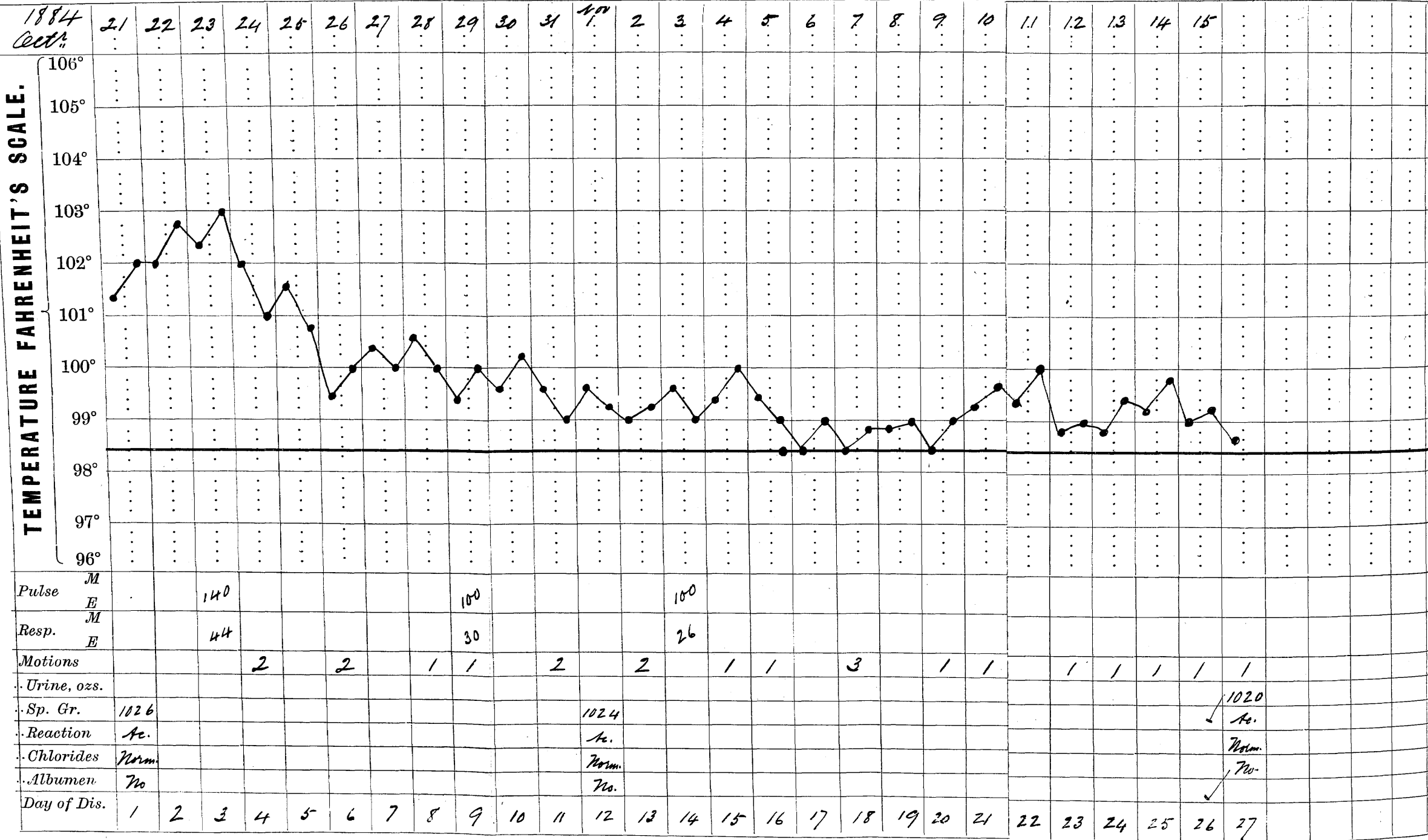
History of a previous attack of "rheumatism"
unaccompanied by fever, 6 mths ago;
and of an attack of acute rheumatism
with affection of several joints, 15 yrs ago.

Treatment pursued - as in Case I.

1st day. Patient free from pain.

Temp: &c normal. Only slight
degree of stiffness in L. Knee.

Name *Thomas T.C.* Age *20.* Disease *Ac. Rheumatism* Result *len* Age



Case III. Thomas R. aet 20.

Ad. 21st Oct. 1884.

Complaining of pain and swelling of the joints of both feet, especially the L. Skin in a state of free perspiration; temp.: $101.4^{\circ}F$; pulse 120. Tongue furred at edges; bowels constipated. Urine moderate in quantity with slight deposit of amorphous urates. Heart and lungs normal on examination.

23rd Oct. The treatment, as in Case I, results in patient now being fairly comfortable.

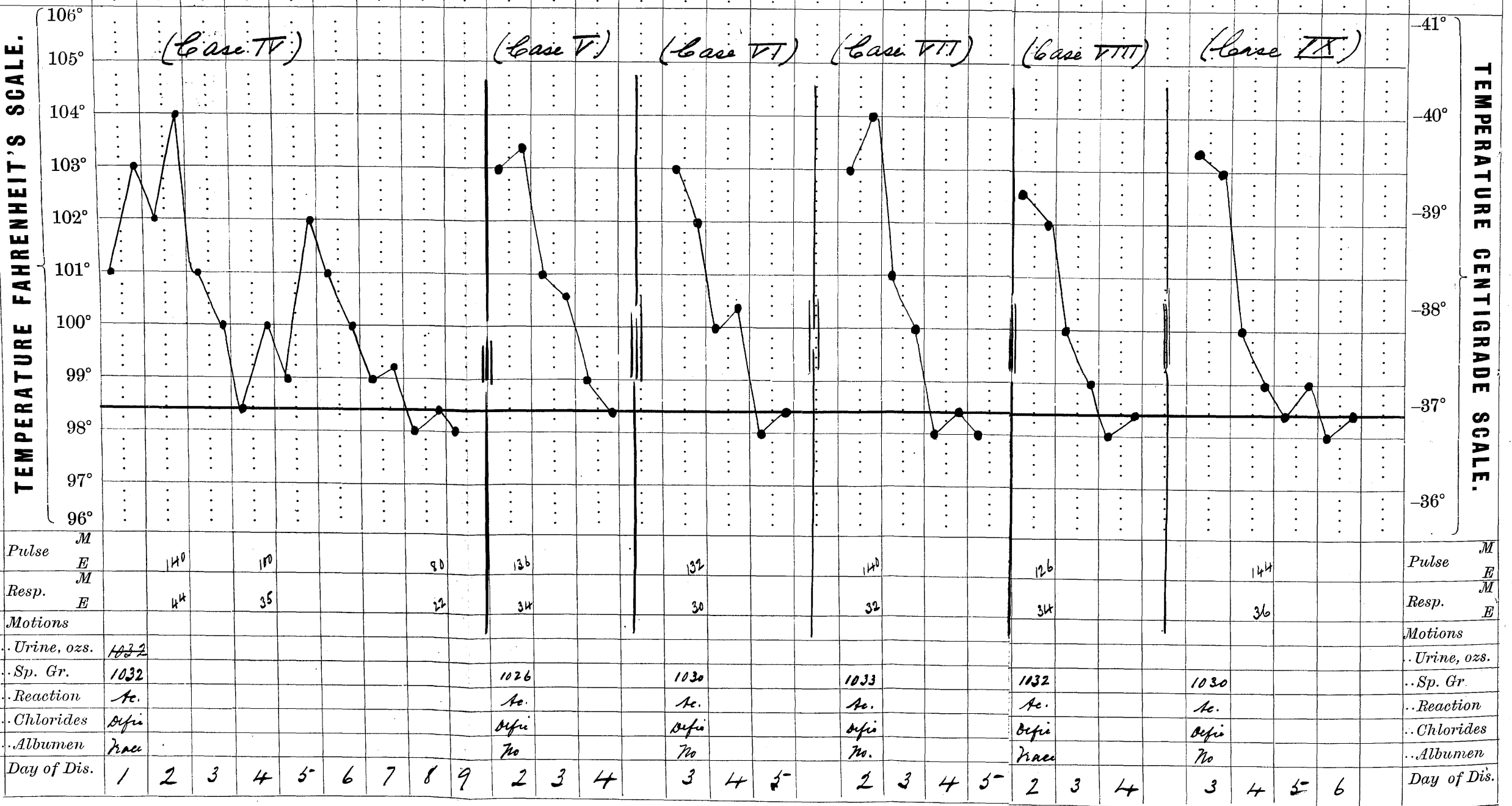
29th Oct. For last 6 days pains have been migrating and troublesome. Cardiac action irregular, but no valvular mischief to be detected. Dose of potash considerably reduced.

20th Nov. Stopped alkaline mixture and prescribed tonics owing to cardiac depression.

6th Dec. Patient well.

Names Wm 7; Mary E. P.; Mrs. H. Ages 16; 25; 28; Disease Ac. Rheumatism Result Cure Result

Wm H., Maggie P. & Robt. G. 23; 37 & 15



7.
Cases IV to IX inclusive.

These six cases on admission all showed the ordinary symptoms of acute rheumatism, - high temp., perspiration and painful swollen joints.

One case had pericarditis on admission and another developed a systolic murmur (mitral) during treatment.

In one case albumen was found in the urine on admission, and in two others traces were occasionally found.

Treatment. Salicin was given, - 25 grs every 2 hrs for the first 24 hrs; 25 grs every 4 hrs for the next 3 days; at the end of the first week, 7 gr. doses thrice daily for 3 days, and then stopped.

In Case I (temp. chart) Salicin was started on the second day and stopped on the fourth owing to headache and noises in the ears causing partial deafness; but

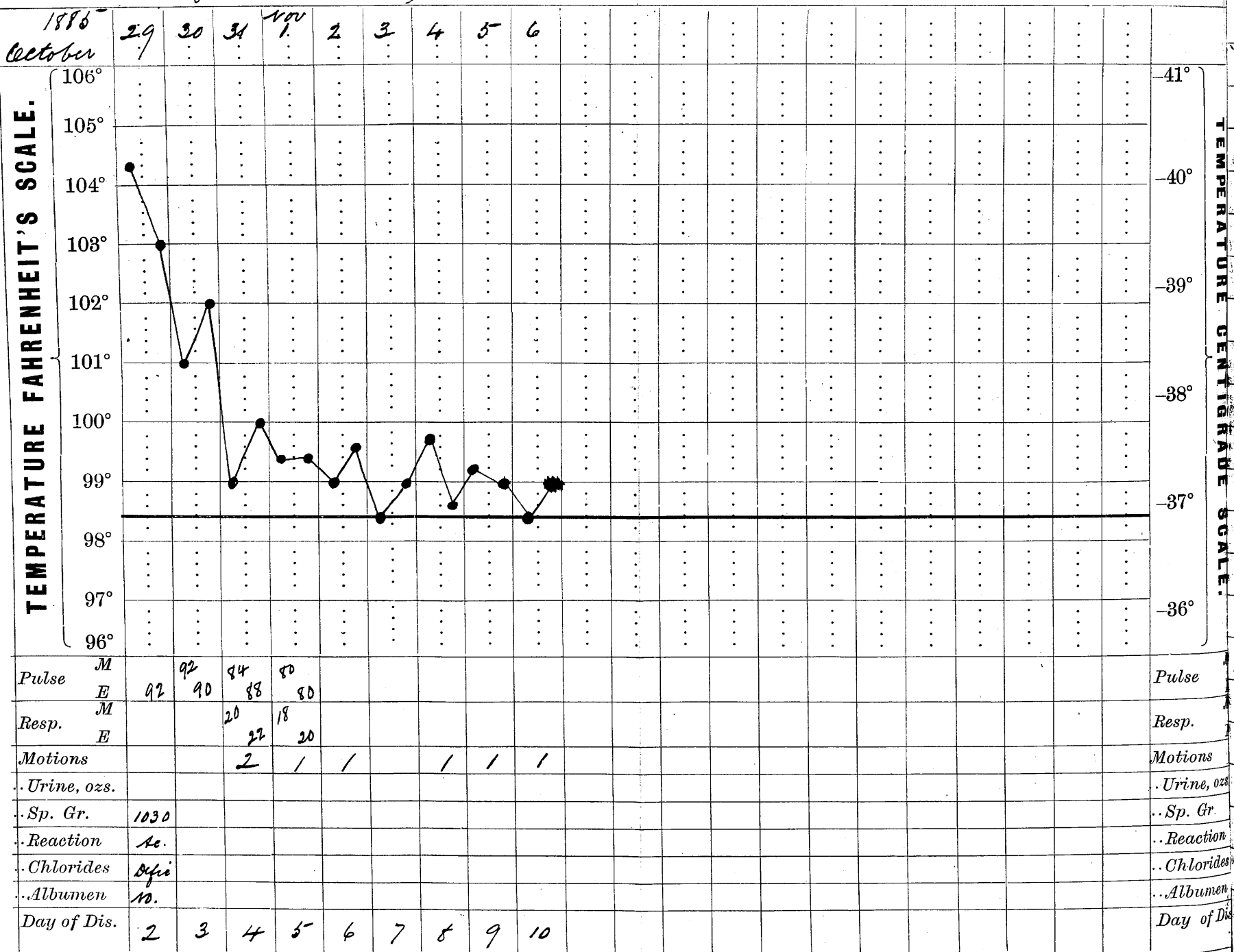
was resumed on the ~~fifth~~ day in slightly smaller doses with good results. The usual hygienic and dietetic treatment pursued in all the cases.

In the six cases the temp^r was reduced to normal at the end of two days treatment, and, simultaneously with it, alleviation of the pain.

Excluding case I, in two out of the five cases, slight stiffness remained in the knees and hands; and in one there persisted some effusion in the R. knee with pain on attempted movement.

At the end of a week, in all six cases, pain and synovial effusion had gone. The skin was natural to the touch; temp^r, pulse and respirations normal; tongue clean, or with very slight fur remaining on the edges, and

Name *George C. (Case I)* Age *18* Disease *Acute Rheumatism* Result *Cured*



76
appetite fairly good; bowels acted naturally, and urine copious and free from amorphous deposit. At the end of a fortnight the pulse began to be feeble in two of the cases, but in none was it irregular in rhythm.

The patients improved rapidly under tonics and were fairly convalescent in from three to four weeks.

Case X. George C., age 18.
 Ad. 29th Oct. 1885.

Complained of pain in knees. Patient in a state of free perspiration; temp. 104.5°F ; pulse 92; urine scanty and loaded with urates. Ankles, knees and wrists were also affected. Heart and lungs normal to physical examination.

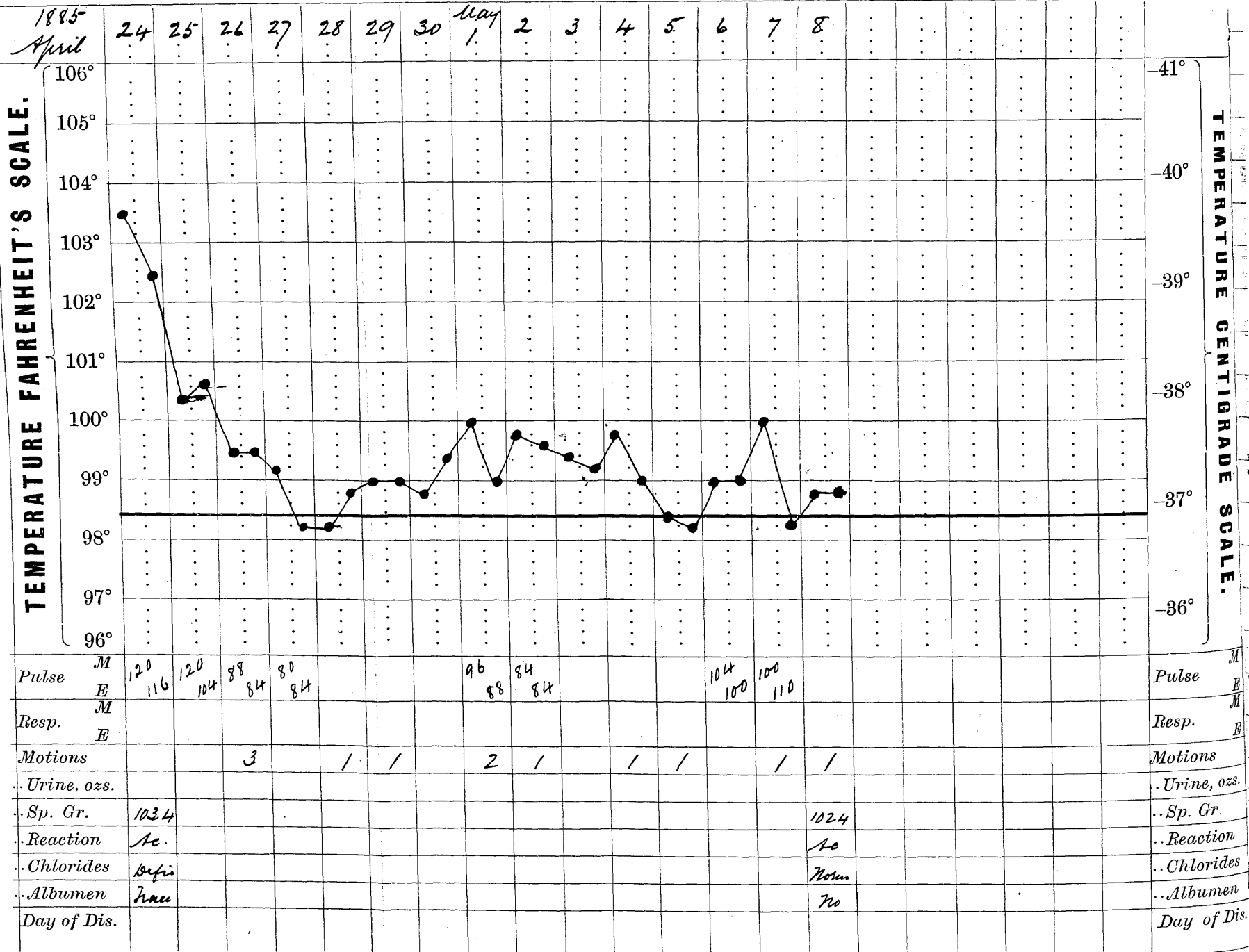
Treatment:- Salicylic acid in 20 gr doses every 4 hrs.

30th Oct. Temp. 102°F ; pulse 78; pain diminished. Patient been sick once and vomited. Ordered Salicylic acid to be continued in 10 gr doses.

31st Oct. Great improvement in temp; pulse, urine &c. Appetite fairly good and tongue cleaning. Pain gone. No cardiac complication.

6th Nov. Discharged convalescent.

ended



Case XI. Kate R., aet 24.

Ad. 24th April 1885.

Suffering from intense pain in knees
ankles and R. wrist. The affected
joints are red and swollen, and the
skin in a free perspiration.

Tongue is furred, bowels loaded and
urine scanty and high coloured.

Slight bronchial catarrh present, and
heart normal to physical examination.

Prescribed salicylic acid in 20 gr
doses every two hours.

30th April. Patient very comfortable.

Prescribed the acid thrice daily.

6th May. Pain returned to R knee and
L wrist. Prescribed 20 grs of the
acid every four hours.

9th May. Stopped the drug on account
of its causing delirium, and gave
alkalies (for four days).

13th May. Convalescent. Has made fair
progress; no more delirium or cardiac
complication.

Case XII. John P. aet 28
Ad. 20th August 1886.

Suffering from painful swelling of the
L. elbow and both knees, said to be
due to exposure to cold and wet.

Tongue furred; bowels constipated;
and urine scanty and high coloured.

Cardiac exam. reveals a systolic
murmur at the apex.

22nd Aug. Pain gone. Free perspiration.

Patient complains of buzzing in the
ears and slight headache. Ordered
the acid, which had been prescribed
at first in 20 gr. doses every three
hours, to be given thrice daily.

24th Aug. Marked deafness set in;
but otherwise patient free from all
troublesome symptoms. Medicine
ordered, - 10 grs. thrice daily.

28th Aug. More or less delirium and
sleeplessness for the last three days.
Pulse laboured and slightly irregular.

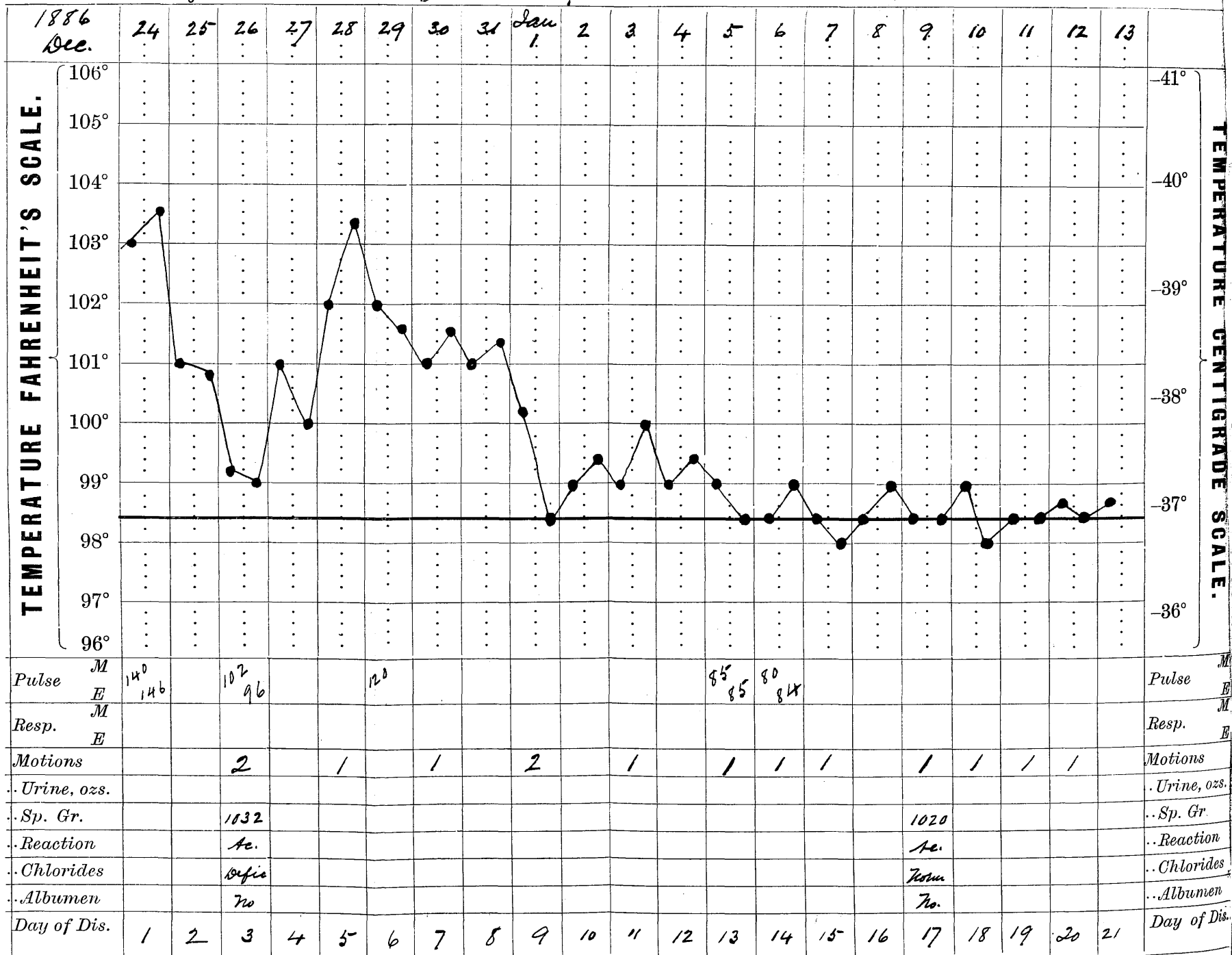
79.
Patient very prostrate. Urine pretty
copious and of a greenish hue,
neutral in reaction, no albumen.
Salicylic acid stopped.

30th Aug. Thrus, ankles and R. wrist
swollen and painful. Prescribed
potash salts, and local sedatives to
joints.

3rd Sept. Patient has shown a
gradual improvement since last note.

10th Sept. Discharged Convalescent.

Name *George H. (Lease XIII)* Age *39* Disease *Acute Rheumatism* Result *Cured.*



TEMPERATURE CENTIGRADE SCALE.

Pulse
Resp.
Motions
Urine, ozs.
Sp. Gr.
Reaction
Chlorides
Albumen
Day of Dis.

Case XIII George H. aet. 39.

Ad. 24th Dec. 1886.

Suffering from severe pain in feet, knees and L. shoulder. Patient flushed, and perspiring freely; temp: 103°7; pulse 140; tongue furred and bowels confined. Attributes his present illness to getting wet while working out of doors. Lungs and heart normal to physical examination.

Treatment:- rest in bed between blankets; milk diet; salicylate of potash prescribed in 15 gr doses every four hours.

26th Dec. Pain much relieved. Still perspiring slightly; temp: and pulse improved. Urine loaded with urates. No cardiac or pulmonary involvement. Eruption of milaria on back.

28th Dec. Patient has had a bad night, owing to recurrence of pain in knees and ankles. Temp: again

up to $102^{\circ}7$; pulse 120; respir. 50.

Skin is hot and dry. Patient complains of inability to lie on R. side.

On examination the base of the L. lung is found dull on percussion, while fine crepitations with prolonged expiratory murmur are heard.

Medicine ordered to be continued with stimulants, and poultices to the back.

29th Dec. Patient had a fair night's rest, and is now perspiring freely.

The R. ankle is swollen, but painful only on attempted movement.

1st Jan. Condition of lung improved, and patient fairly comfortable.

Ordered the Salicylate thrice daily.

5th Jan. Temp. $99^{\circ}7$; pulse 85, very weak and irregular in rhythm.

Stopped the salicylate & potash.

20th Jan. Temp. normal since last record. Patient fairly convalescent.

Name

George P. (Case XIV)

Age

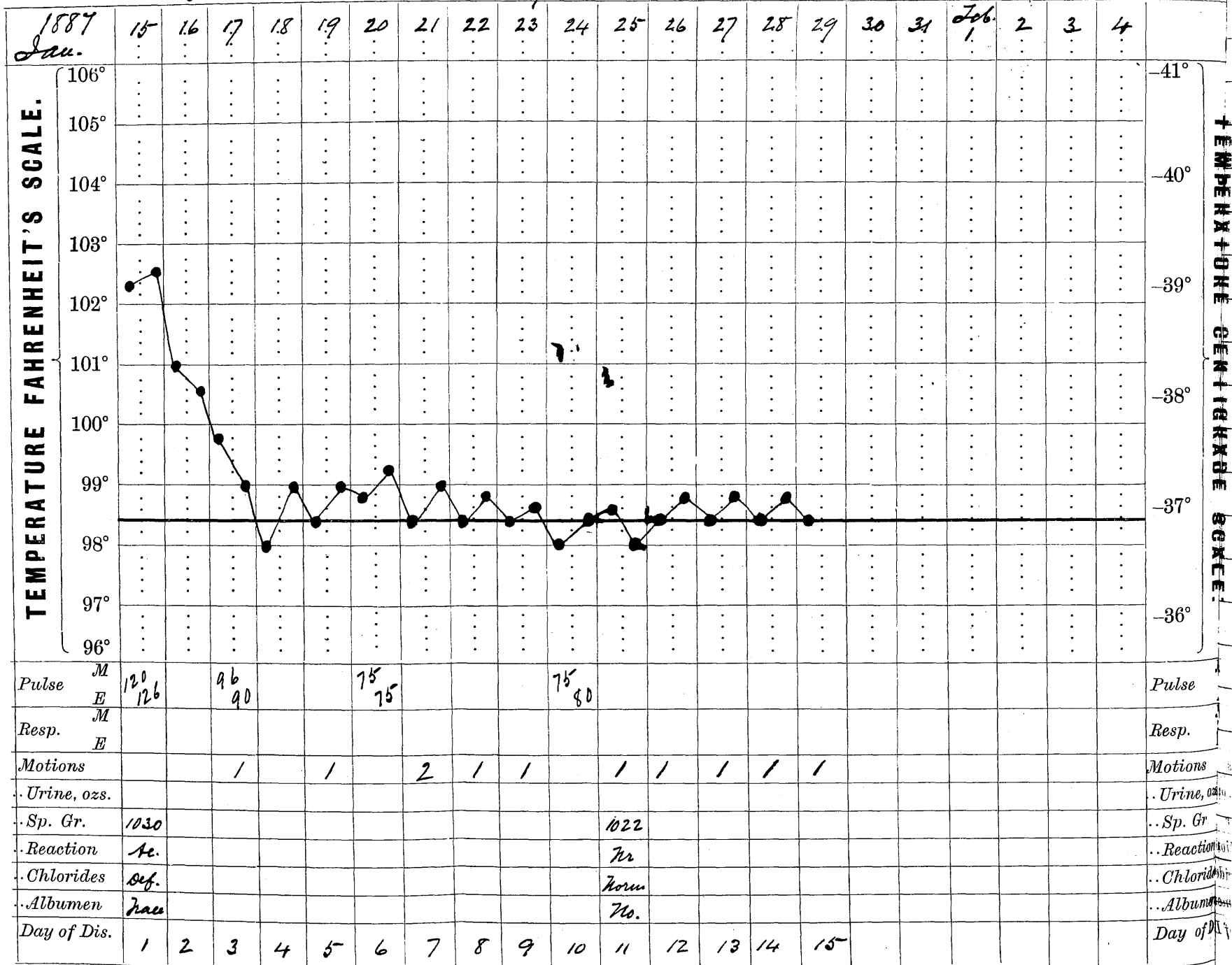
27

Disease

Acute Rheumatism

Result

Cured.



Case XIV.

George P. aet. 27.

ad. 15th January 1887

Found patient suffering from a moderately severe attack of acute rheumatism. Pains in hands and knees. The R. Knee is much swollen. Skin moist, and tongue furred.

Prescribed salicylate of potash in 15 gr doses every four hours.

17th Jan. Pain almost all gone. Temp: 99.8°F, pulse 96.

18th Jan. Pain gone. Temp: normal. Ordered the salicylate to be continued three daily.

26th Jan. Temp: normal since last record. Pulse weak and intermittent. Salicylate stopped and stimulants given with iron and quinine.

10th Feb. Patient discharged well.

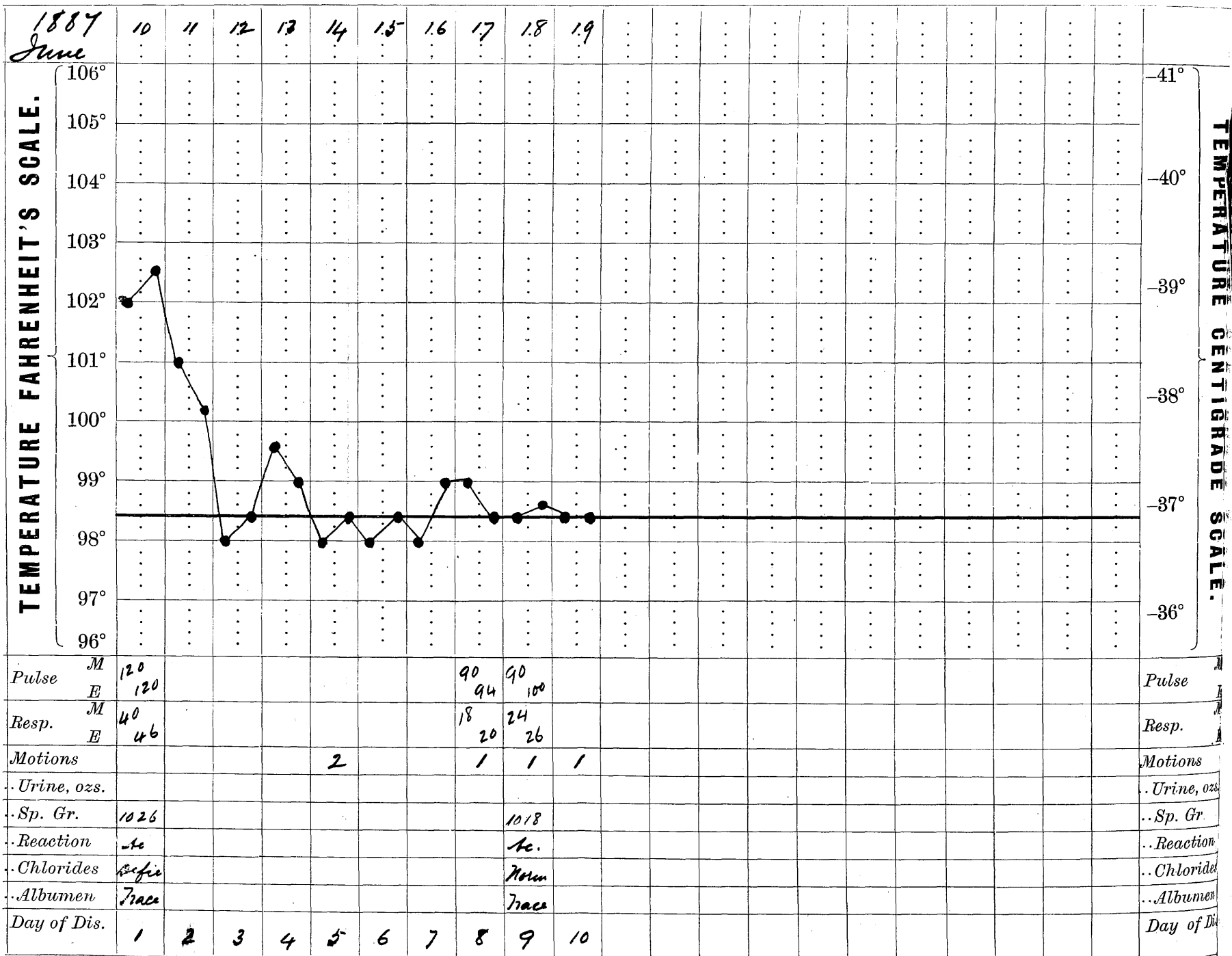
Name *Ellen B. (Case XV)* Age *14*

Age 14

| | | | |
|---------|------------------|--------|--------|
| Disease | Acute Rheumatism | Result | Cured. |
|---------|------------------|--------|--------|

Result

bund



Case XV. Ellen B. aet 14.

ad. 10th June 1887.

A moderately severe case of acute rheumatism in which the joints chiefly affected are the wrists and shoulders. Skin moist; temp. 102°F ; pulse 120 and full. Tongue furred. History of a previous attack three yrs ago, similar to the present, and followed by Chorea.

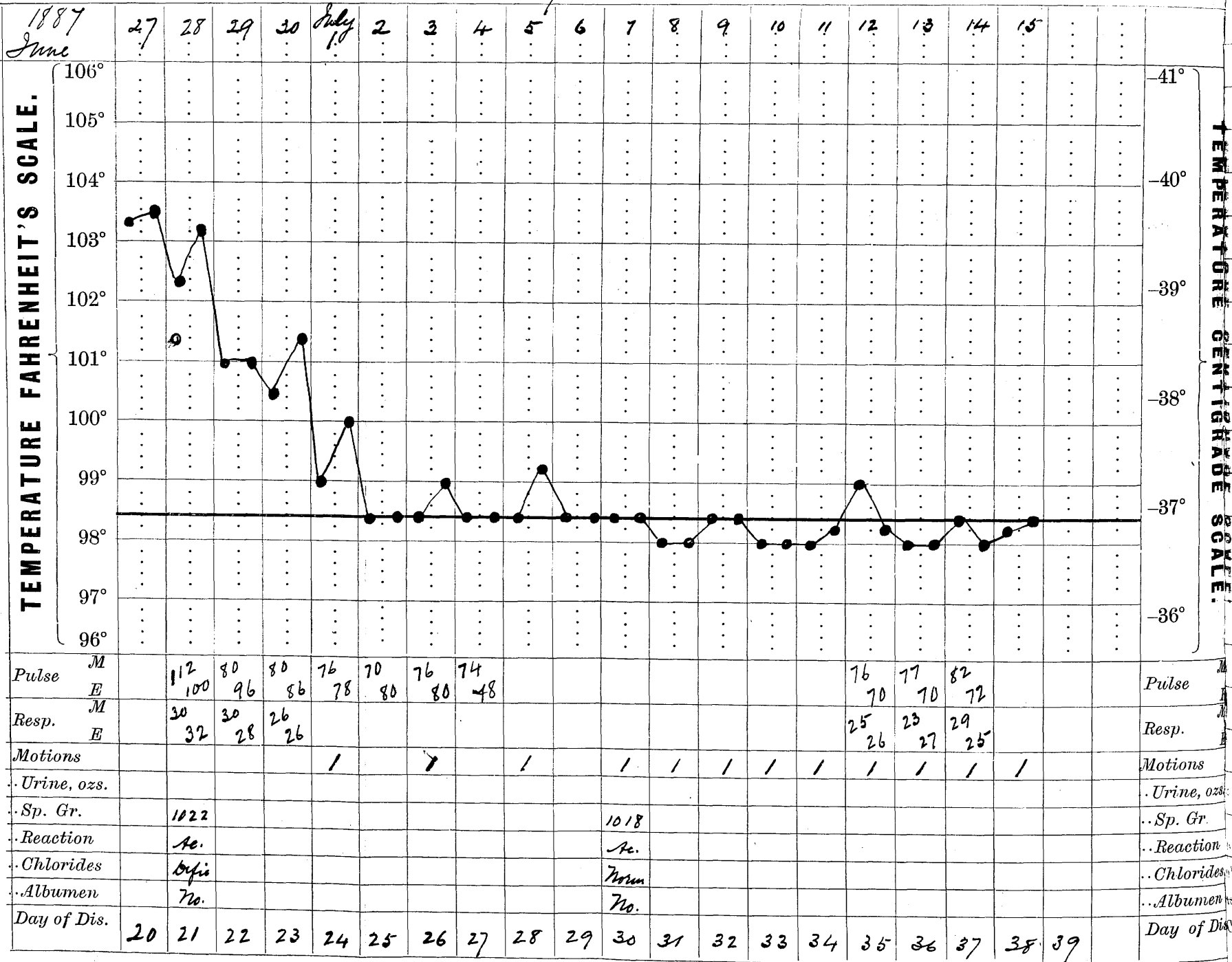
Lungs normal. Rough systolic murmur present in mitral area with increased cardiac impulse.

Prescribed salicylate of potash in 10 gr doses every four hours for three days; then three daily for ten days; then iron and arsenic.

In less than three days pain and fever had subsided, and patient made an almost constant progress towards convalescence.

Name *Martin M. (Case XVI)* Age *27*

Disease *Acute Rheumatism*

Result *Curd.*


Case XVI. Martin M. aet 27.

Ad. 27th June 1887.

Patient states that he had been ill three weeks before admission with migrating pains in the larger joints.

When seen he complained of pain chiefly in the wrists, R. knee, and L. ankle. The skin bathed in perspiration, with large crops of miliaria over the chest and back. Urine scanty and free from albumen; depositing urates. Heart and lungs appear normal.

Salicylate of soda was ordered in 12 gr doses every four hours.

29th June. Patient appreciably improved.

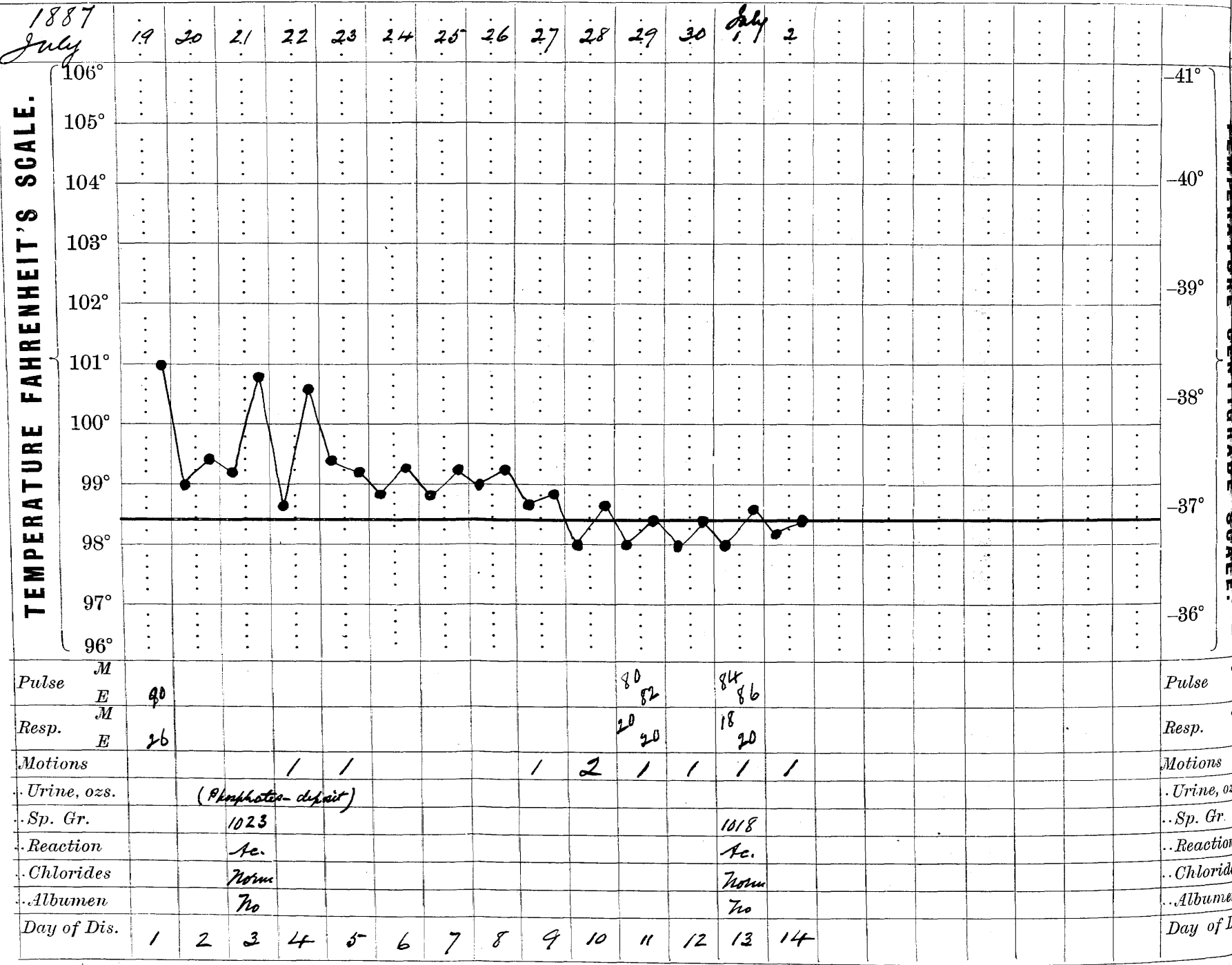
2nd July. Temp: &c normal. Joints quite free from pain or swelling.

Medicine ordered thrice daily.

15th July. Medicine stopped. Not a bad symptom developed.

21st July. Discharged well.

Name *Wm. F. (Lease XVII)* Age *13* Disease *Ac. Rheumatism* Result *Healed*



Case XVII. Ho. W^m F. act 13.

Ad. 19th July 1887.

complaining of pain in the ankles and wrists, which are found swollen.

Skin moist; tongue furred; appetite impaired; bowels confined.

Temp^t. 101° 7; pulse 90; respir^{ns} 26.

Lungs normal to physical exam., but the heart reveals a rough systolic murmur in the aortic area.

History of two previous attacks of a similar nature to the present, all said to be caused by getting chilled in wet clothes.

Salicylate of soda prescribed in 8gr doses every four hours, - 21st July.

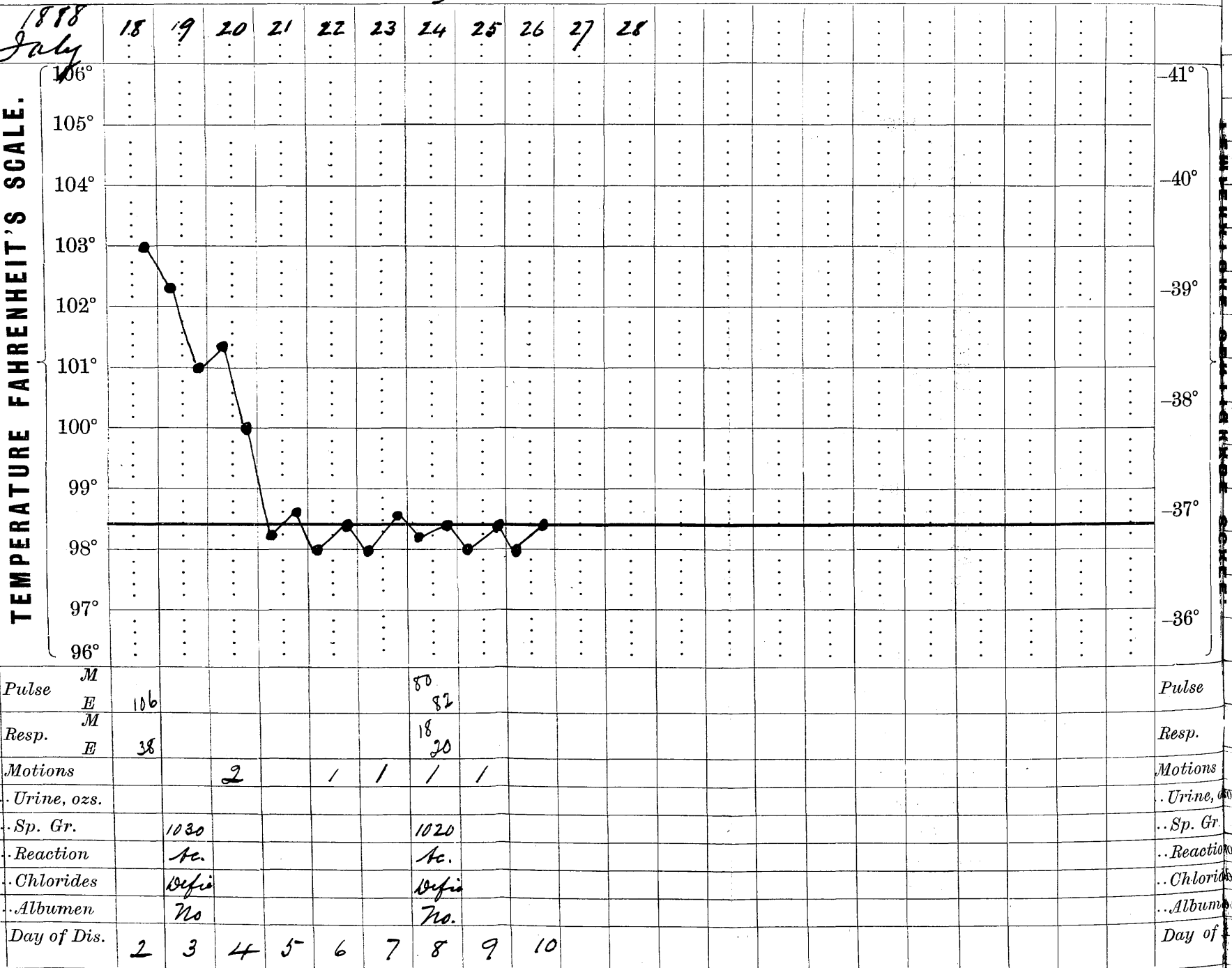
23rd July. All pain gone. Skin natural to touch. Medicine thrice daily.

8th Aug. Discharged well; the salicylate having been stopped for a week, and temp^t. constant at normal.

Name *Michael M. (Case XVIII)* Age *18.*

Disease *Acute Rheumatism* Result *Cured.*

TEMPERATURE FAHRENHEIT'S SCALE.



Case XVIII. Michael M. Oct. 18.
Ad. 18th July 1888.

Complaining of acute pain in the
Shoulders, wrists and L. Knee.

Perspiring freely; pulse full and
bounding, 106; temp: 103° 7; resp^{ns} 38.

No heart or lung complications.

Salicylate of soda prescribed in
12 gr doses every four hours.

21st July. Patient free from pain.

Pulse, temp: and respirations
normal. Slight stiffness in
R. Knee remaining, with pain on
forced movement. Medicine to
be given thrice daily.

3rd August. Salicylate stopped,
and tonics given.

14th Aug. Discharged well.

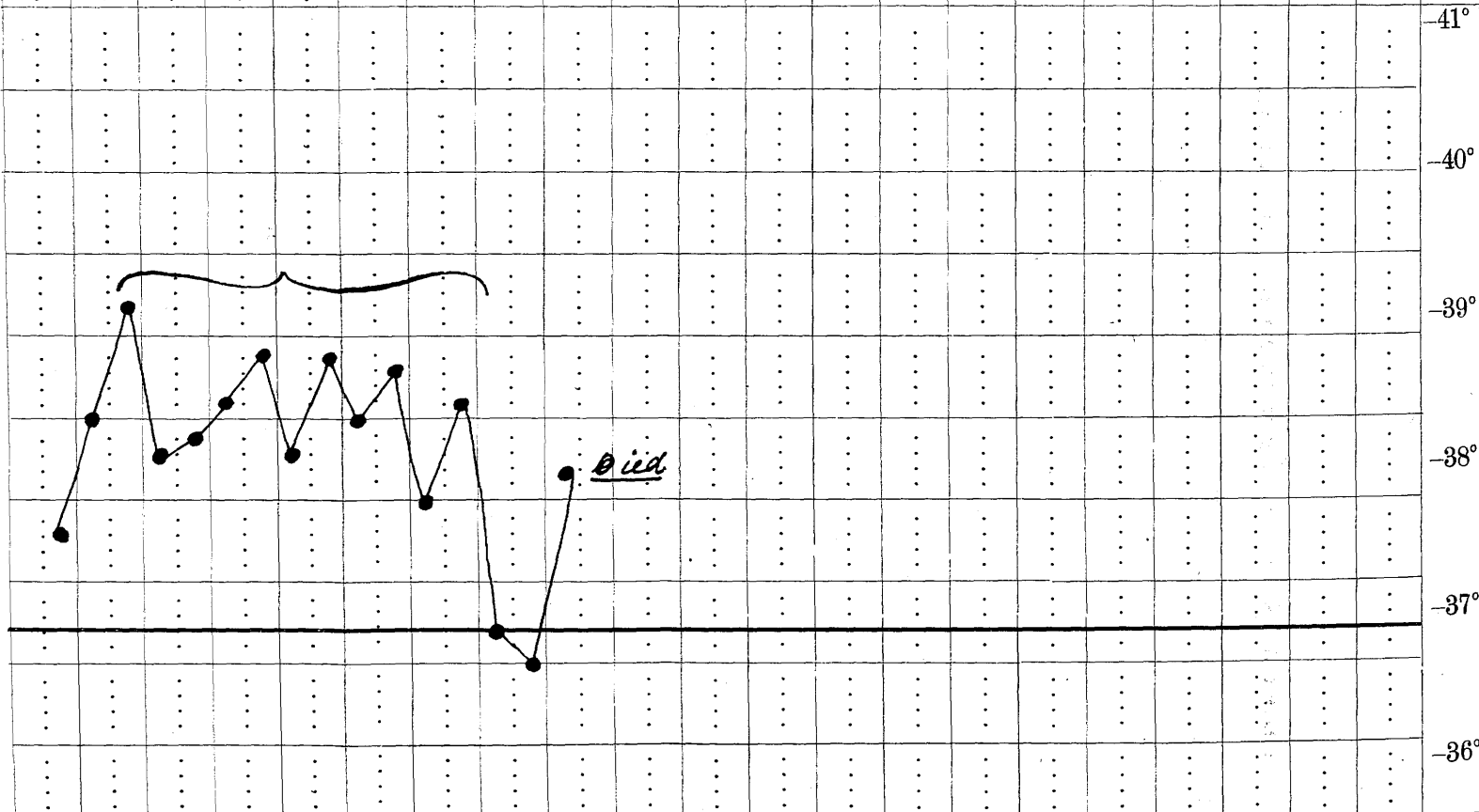
Bases,

XXIX to XXVI (inclusive),
to illustrate special points in
connection with the pathology,
treatment and complications
of acute rheumatism.

Bath.

| | | | | | | | | | |
|----|---|---|---|---|---|---|---|---|----|
| 1. | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|----|---|---|---|---|---|---|---|---|----|

106°
105°
104°
103°
102°
101°
100°
99°
98°
97°
96°



| |
|-------------------------|
| Pulse |
| Resp. |
| Motions |
| .. Urine, ^{or} |
| .. Sp. Gr. |
| .. Reaction |
| .. Chlorides |
| .. Albumens |
| Day of |

Case XIX; resisting treatment; death
on the 9th day. Ad. 1st Jan. 1887.

Ad. W. act 52, a man of intemperate
habits and drinking for some days
before admission. History of three
previous attacks of acute rheumatism.
Complains on admission of shooting
pains in the arms and legs.

2nd Jan. In 24 hours the temp.
has gone up to 102° , and the
pain located in knees, wrists and
R. shoulder chiefly. Perspiring
freely. Tongue very foul; complete
loss of appetite; bowels confined.
Examination of the chest gives
evidence of emphysema. A few
moist râles are heard over the
bases of the lungs. Heart is
dilated and sounds faint and
muffled. Urine scanty, loaded
with urates, bile present and also
albumen.

7th Jan. Patient very depressed. Heart sounds feeble and very irregular. Breathing difficult from engorgement of the bases of both lungs. Salicylate of Soda, which the patient has been taking in 15 grs every 4 hrs since admission, ordered to be stopped.

9th Jan. Patient died.

P.M. Exam. All the organs of the body flabby. Complete adhesion of pericardium to heart from old pericarditis. Cavities of heart dilated. Valves intact, and no sign of endocarditis. Both lungs at their bases in the stage of red hepatization.

| Disease | Endocarditis (rheumatic ?) | Result | Res |
|---------|----------------------------|--------|-----|
| | | | |

| <i>Age</i> | <i>Disease</i> | <i>Result</i> |
|------------|----------------|---------------|
|------------|----------------|---------------|

| | | | | | | | | | | |
|----|----|----|----|----|----|----|----|----|----|----|
| : | : | : | : | : | : | : | : | : | : | : |
| 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 |

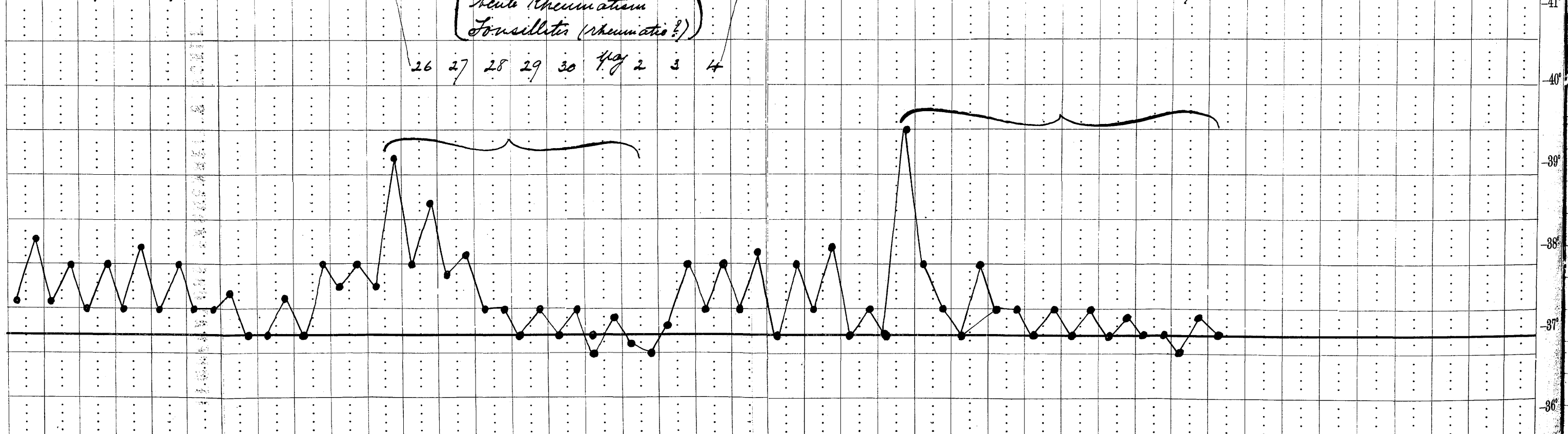
Embolism - cerebral.

Hemiplegia

1 2 3 4

| | | | | | | | | | | | | | | | |
|---|---|---|---|----|----|----|----|----|----|----|----|----|---|---|---|
| : | : | : | : | : | : | : | : | : | : | : | : | : | : | : | : |
| 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | . | . | . |

106°
105°
104°
103°
102°
101°
100°
99°
98°
97°
96°



| Pulse | Temp | Respiration | Motions | Urine, ozs. | Sp. Gr. | Reaction | Chlorides | Albumen | Day of Dis. |
|-------|------|-------------|---------|-------------|---------|----------|-----------|---------|-------------|
| 80 | 86 | 20 | | | 1020 | Ac. | Norm | Trace | |
| 80 | 86 | 20 | | | 1028 | Ac. | Defic | Trace | |
| 80 | 86 | 20 | | | 1028 | Ac. | Defic | Trace | |
| 80 | 86 | 20 | | | 1020 | Ac. | Norm | Trace | |

Case XX. Florence M. aet 15.

ad. 3rd April 1889; suffering from hemiplegia of the L. side.

Cardiac examination, - heart hypertrophied, rough aortic systolic murmur and presystolic and systolic murmurs (obscuring the 1st cardiac sound at the apex) at the mitral area. Lungs and Kidneys apparently normal.

The hemiplegia set in suddenly about 3 wks ago. History of a painful joint affection about 18 mts back, but no direct history of rheumatic fever.

Treatment, - rest in bed, light farinaceous diet, and iodide of potassium in 15 gr doses thrice daily.

25th April. Patient continued to make satisfactory progress. This evening the temp^r rose to 103° F.,

90.
and this simultaneously with pain and effusion in the small joints of L. hand, L. ankle and both knees. Salicylate of soda was ordered in 10 gr doses three daily.

2nd May. Pain gone in about 48 hrs. Temp^r now normal. Stopped the salicylate, owing to the patient being sick and vomiting twice. Prescribed iodide of potash again.

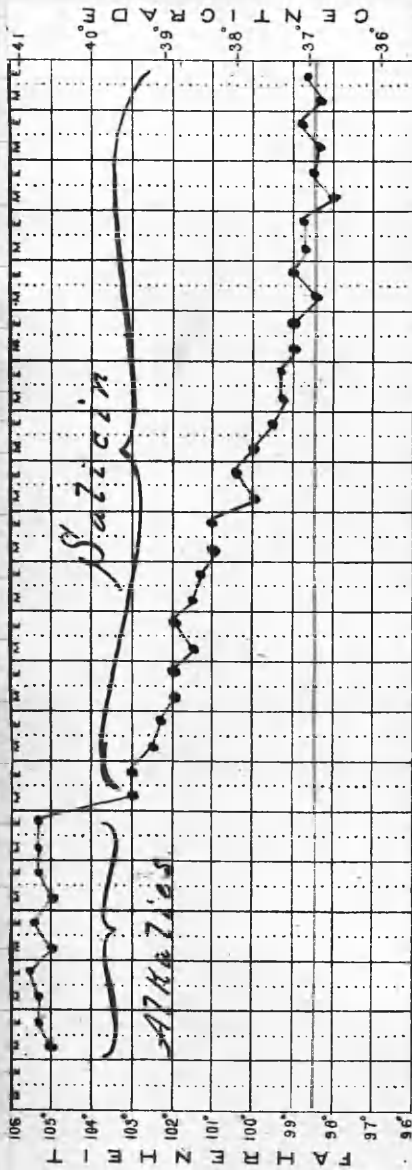
9th May. Temp^r slightly raised since salicylate stopped. Temp^r went up this evening to 103° F. No joint affection; but patient complains of difficulty in swallowing solids. Examination of the throat shows both tonsils inflamed acutely and enlarged. No false membrane or exfoliation.

Prescribed salicylate of soda and gargle for throat.

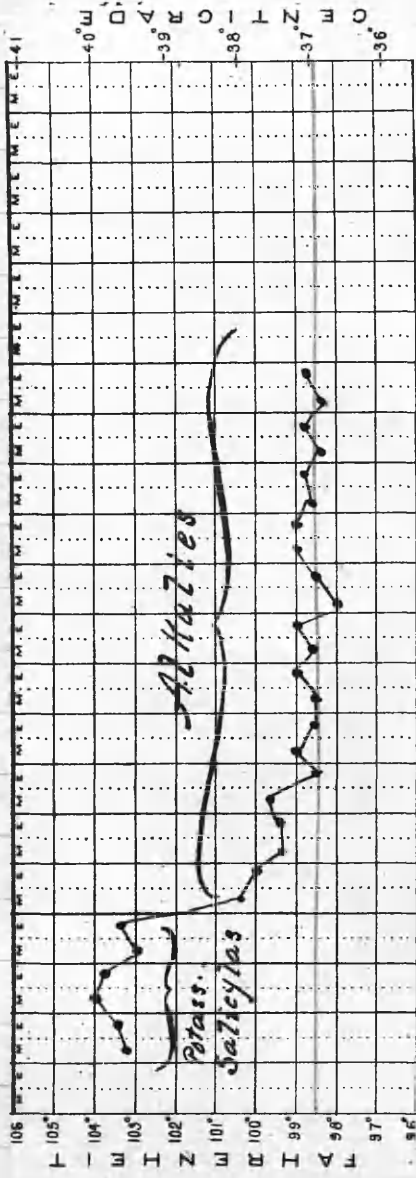
11th May. Throat much better

18th May. Temp^r normal. Stopped medicine.

base
XXI



base
XXII



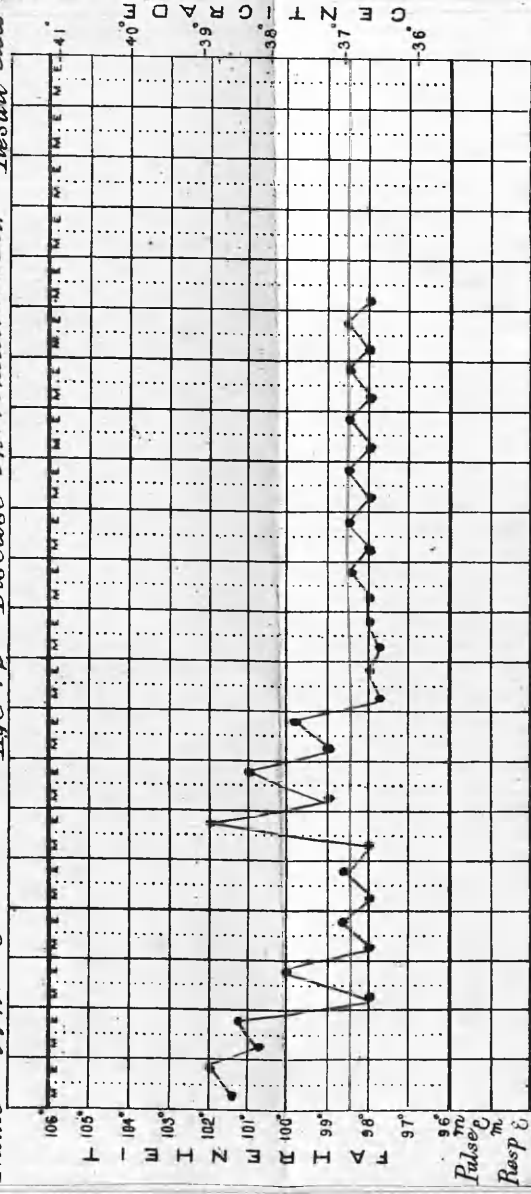
Case XXI. Temperature chart showing the course of fever in a severe case of acute articular rheumatism, without any special complications.

Treatment was started with large doses of potash salts, and carried on for four days without benefit.

Salicin was substituted, with the result of gradual and steady improvement.

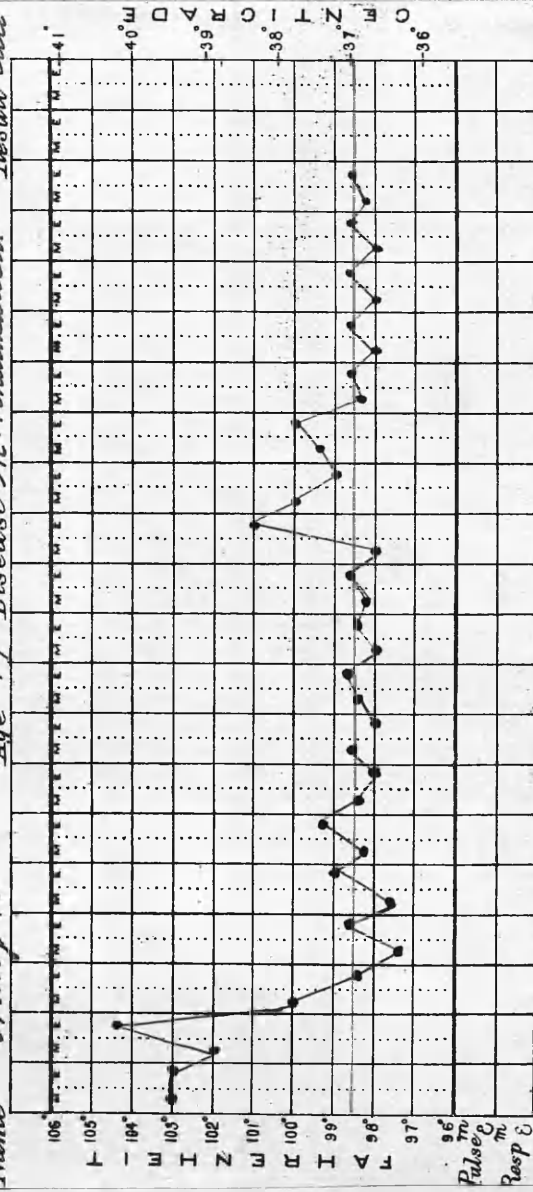
Case XXII Temperature of case which was first treated by salicylate of potash, which exhibited its physiological symptoms without abating the fever. The substitution of alkalies gave almost immediate relief which was maintained.

Name John J. Age 16 Disease Ac. Rheumatism Result Cure



base
XXIII

Name Harry K. Age 19 Disease Ac. Rheumatism Result Cure



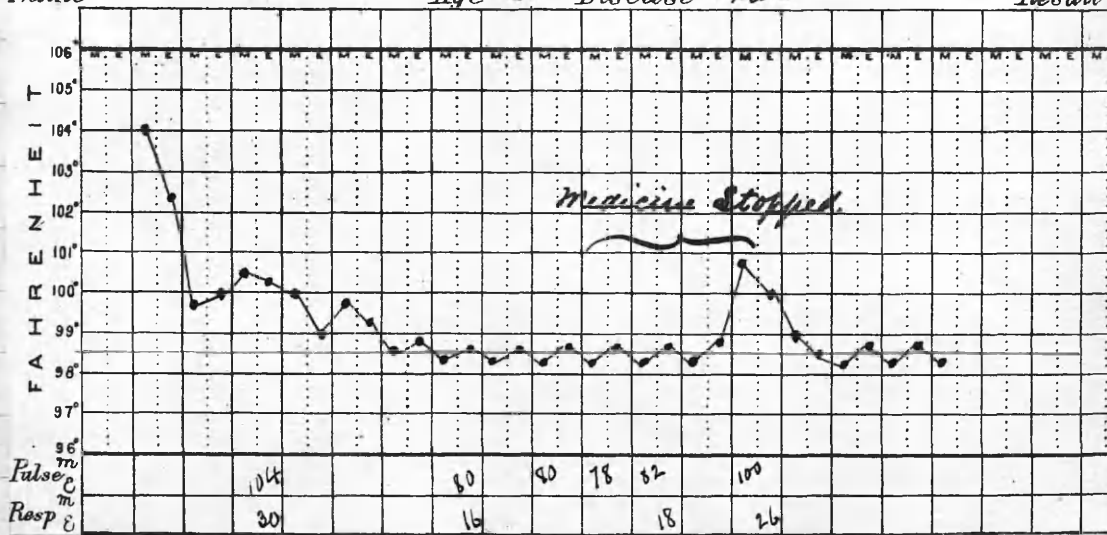
base
XXIV

Cases XXIII and XXIV. These temperature charts are introduced to show relapses occurring in the progress of each case in spite of the continued use of salicylic acid as a therapeutic agent, and the adherence to milk diet and rest in bed.

These cases are interesting in the light of the question as to their being a distinct form of acute rheumatism which tends to relapse in spite of all that the physician can do for the patient. In my cases I have never found more than one relapse occur, while the patient was strictly under treatment, and that usually at the end of the first or in the second week of the illness.

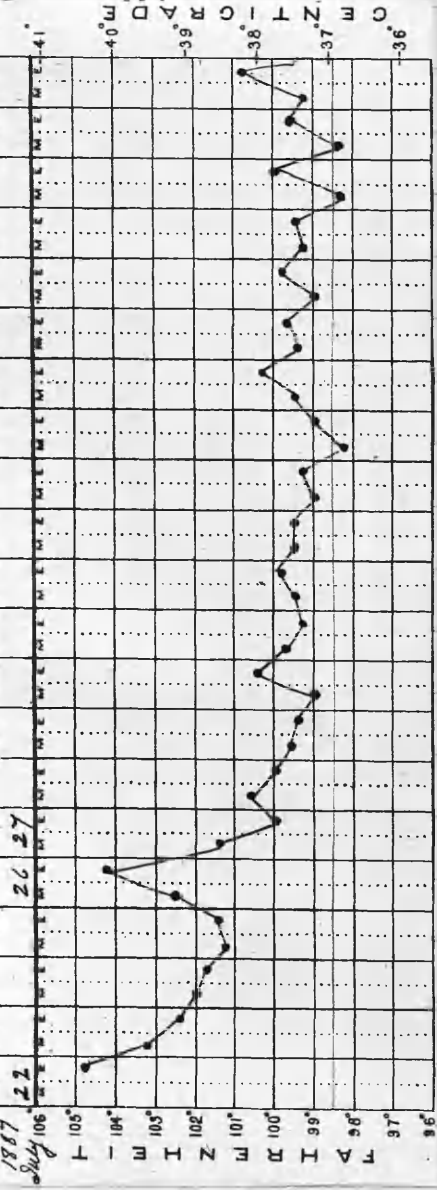
Case XXV.

Name *Joh. B.* Age *25* Disease *Acute Rheumatism* Result

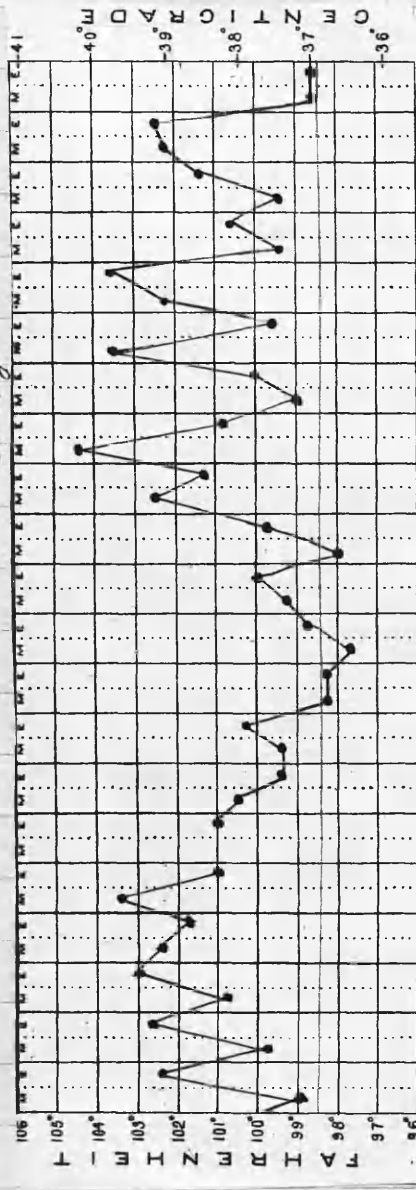


Case XXV shows a temperature chart with a relapse occurring on stopping the salicylate of soda too soon. The case was an ordinary uncomplicated one of acute rheumatism, treated by salicylate of soda in 12 grs every four hours, until the temp^r was normal; then, thrice daily for four days. Two days afterwards the temp^r rose, with return of symptoms, and on the third morning reached nearly $101^{\circ}7$. By renewing the salicylate and continuing it for ten days longer, the patient made an uninterrupted recovery.

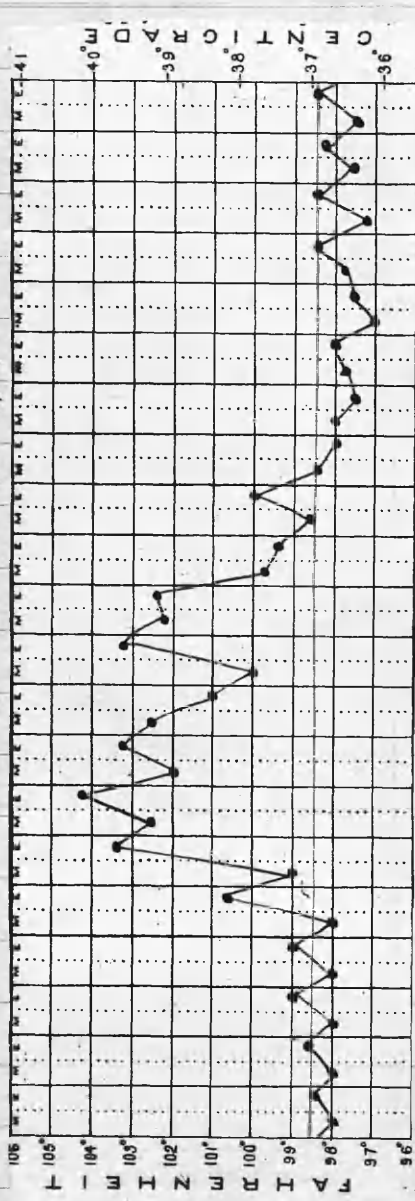
Name Jane L. Age 23 Disease Rheumatic Endocarditis Result Cur.



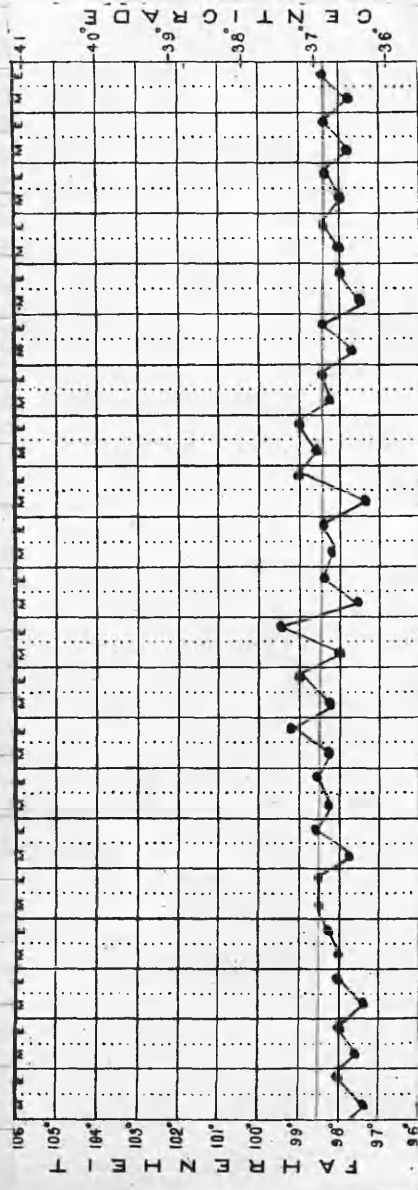
25th Aug.



15th Sept.



8th Oct.



Case XXVI. Same C. art. 23.

Ad. 22nd July 1887 to Hospital, in an apparently dying state, after having been suffering from acute rheumatism at home for about seven weeks.

Skin moist in a filthy condition.

No joint pain. Temp: $104.8^{\circ}F$; pulse irregular; resp: 40.

Cardiac sounds muffled by murmurs at apex and base; but exact rhythm unable to be diagnosed owing to weakness and irregularity of action.

Urine acid, and containing a fair quantity of albumen.

After having a warm alkaline bath, patient was put to bed between blankets and fed with milk. Salicylate of soda was prescribed in 15 gr doses every four hours.

26th July. The temp: which had

gone down to 101.2°F , has now risen
 to 104.2°F . in spite of the continued
 administration of the salicylate.
 Patient is unconscious. Urine drawn
 off with catheter. Subcutaneous
 tenderness and floccitatis already
 developed. Fortunately the
 patient has never been troubled
 with stomach complications.

10 gr. Quinine given, followed up
 after 6 hrs by 5 grs every 4 hrs.
 Fed every 10 minutes with
 beef tea, milk, eggs and brandy.

27th July. Temp^r down to 100°F .

Great improvement all round.

25th Aug. The temp^r, which
 has been kept down by
 regular doses of quinine 5 grs
 three daily, with occasional
 large single doses, has again
 risen to 104.4°F . It is thought
 advisable to try Antipyrine in

20 gr. doses.

13th Sept. The effects of the antipyrene have been found to be very evanescent; a reduction of from 3° to 4° 's being easily got in 8 hrs, but followed by quite as rapid a return of the fever.

Salicylate of Quinine is now tried in 2 gr. doses thrice daily.

8th Oct. Since last note patient has steadily improved, without a single bad symptom.

Cardiac examination now shows a systolic murmur in the aortic area, and a rough presystolic and systolic obscuring the first sound in the mitral area. (During the course of the illness murmurs at intervals could be heard at all the orifices of the heart, varying in degree and character from time to time).

20th Oct. Discharged convalescent.

Results.

It is now established beyond all possible reputation that the Salicyl compounds are of the greatest value in the treatment of acute rheumatism, and as such deservedly occupy the chief place in our estimation for that purpose.

At the annual meeting of the British Medical Association in Dublin, 1887, Prof. Gairdner^a remarked, in the course of his address, that;—the benefit derived from the salicyl compounds in acute rheumatism was to his mind very satisfactorily established, and he should be personally

^a British Med. Journal; Aug. 1887.

disposed to claim this as a very distinct advance in the healing art within a comparatively recent period, and a partial removal moreover of one of the old "opprobria medicinae" which he had been obliged over and over again to recognise as such.

Results. The results of treatment indicate that no special remedy or line of treatment could absolutely be depended on to cure or even give relief to the patient; nor indeed ought we to expect so much. Age, habits, idiosyncrasies, complications, &c. all play their parts to such an extent as to warrant special attention, and only by their careful study and consideration, as well as by an exhaustive inquiry into the pathology of the disease, can

reasonable data be furnished for treatment. The physiological action of drugs on the healthy subject, in many cases unfortunately, is of no practical advantage to the physician, yet, in association with their therapeutic actions, deserves attention. The therapeutic action may even be found to vary within very wide limits.

The danger, of mistakes arising from treating "the disease" instead of "the perturbed state of the bodily functions", is great; hence it is impossible to find a particular line of treatment applicable to all cases.

When rules are laid down, they should be carefully considered as the "best on the whole for the most ordinary uncomplicated form of the affection"; and then

pathological and therapeutical knowledge should be brought to bear specially on the other cases as to the line of treatment to be pursued.

Pain.

The relief from pain is to the patient of so much importance that, with it, the disease is more than half overcome. Of all remedies used for acute rheumatism (not taking into account the obtaining of temporary benefit from narcotics), the salicyl compounds claim precedence in respect to the speedy relief afforded.

As a rule the pain disappears with the subsidence of the fever, or slightly in anticipation of it. The different salicyl preparations appear to have as nearly as possible the same effects.

Skin.

The result of treatment on the secretions of the skin is rather uncertain and erratic. The sour-smelling perspiration, so characteristic of acute rheumatism, has long been looked on as an effort of nature to get rid of the morbid products. But, the relief from troublesome symptoms is by no means in proportion to the amount of sweat exuded. Salicylic acid and salicylate of potash generally increase the amount of perspiration, while salicin and salicylate of soda have no appreciable effect on the quantity secreted. All the salicyl compounds act in preventing the perspiration in decomposing on the surface of the body and becoming acid.

Temperature.

The rapid reduction of the high temperature is the chief therapeutic result of the salicyl compounds. In this they are all efficacious; the fever subsiding in from two to three days after starting the treatment.

Heart.

When the temperature falls to normal the cardiac action becomes moderated, and the tendency is ultimately, if the drug be pushed, to produce more or less depression. The potash salt usually causes intermittent action after the end of the second week of administration. Salicin, being more of a tonic than the salicylates, rarely causes any cardiac depression. The soda salt, however, can

be very easily regulated so as to avoid the depression often associated with it in practice. When alkalis are given in conjunction with the salicylates of potash or soda, the tendency to irregularities in force and rhythm of the pulse is increased. The salicyl compounds have no direct action in preventing cardiac complications arising in the course of treatment, but, by arresting the morbid action on the tissues, probably arrest what is believed to be an analogous action on the cardiac structures.

Respirations.

The respirations seem to rise and fall directly with the temperature. With chest complications they vary according to the nature and severity of the symptoms.

Muscular & Nervous systems.

These being so intimately associated must be considered together. The implication of the muscles is generally more real than apparent, as they may be observed to atrophy often out of all proportion to the rest imposed on them by the joint affections. This subject has lately been ably worked out by Dr. J. S. Bury², who points out the prevalence of atrophic changes in the muscles associated with the affected joints, and even after the patient is fairly convalescent. The rapid wasting seen during convalescence is probably due to the direct action of the rheumatic virus on the terminal nerve elements, which again react on the muscles. Treatment has not yet been proved to have any

a. Medical Chronicle, June 1888.

appreciable influence on this process, though this is probably owing to our imperfect knowledge of the rheumatic pathology.

Delirium (said by Th. Simon^a and Lendet, to be due to implication of the heart: though denied by Besnier^b) is really an almost unknown factor in an uncomplicated case of acute rheumatism when treated judiciously by salicin or salicylate of potash.

Dr. Wilks^c "so-called" "cerebral rheumatism" *** facsimile of delirium tremens", I believe to be sometimes due (at least in part) to impure preparations of salicylic acid containing phenol and carbolic acid. The chief cause is probably an affection of the serous coverings of the brain

a. Dechambres Encyclopédie; art. Rhumatisme.

b. Report to Clinical Society; 1877.

c. "Diseases of Nervous System; 1878.

of a nature comparable with the hyperaemia of the fringes of the synovial lining of the joints.
Gastro-intestinal.

Irritation of the gastro-intestinal mucous surfaces may occur from the use of any of the salicyl Compounds. The most liable in this respect is the acid which may cause burning in the throat, sickness and diarrhoea.

Salicin may cause vomiting sometimes, but from the largeness of the dose requiring to be given, more than anything else. It is certainly not a direct irritant. The soda salt, though really more irritating than salicin, is better borne, as the dose required for therapeutic purposes is so much smaller of the former.

Urinary.

The scanty secretion of urine loaded with urates, and often with a trace of albumen in addition, is a common phenomenon in the acute stage of a rheumatic attack.

With the departure of the acute symptoms the quantity of urine increases, the sp. gr. becomes lower, urates disappear, and the chlorides (which are always diminished during the acute stage) return to their normal proportion in the urine. The presence of albumen does not contraindicate salicyl treatment, though the kidney symptoms are sometimes aggravated by impurities in the specimen of salicylate used.

Conclusions.

General.

- (I) The prognosis in chronic cases is much more favourable than in acute.
- (II) The discomfort to the patient is in direct ratio generally to the chronicity of the disease.
- (III) Ameniability to treatment is generally in direct ratio to the acuteness of the disease.
- (IV) Complications and relapses occur in indirect ratio to the vigour of the patient and the care exercised during treatment and convalescence.
- (V) No remedy is infallible in all cases.
- (VI) Complications must be treated, as such, when they arise.

Special.

- (I) The patient should lie between blankets. Food :- milk, followed by farinaceous food and beef tea. Regulate bowels by Salines. Stimulants may possibly be required to relieve depression. For thirst give lemonade or imperial drink. Diet during Convalescence :- Soup, fish, Chicken and mutton.
- (II) No remedy is infallible in all cases, but the salicyl compounds are superior to all other remedial agents in the treatment of acute rheumatism.
- (III) In the great majority of cases salicylate of soda is more certain in its action than salicin, easier to administer (on account of its greater solubility, and smaller dose required), and no more dangerous in its action when

carefully prescribed; while, it is free from the depressing action of salicylate of potash and the irritant action of salicylic acid.

(IV) In ordinary uncomplicated cases of acute rheumatism salicylate of soda should always be first tried.

(V) It is best employed in moderately small doses, — 8 to 15 grs — every four hours until the temp. is normal, and gradually lessened.

(VI) The subsidence of the fever is the indication for lessening the amount and frequency of administration of the drug.

(VII) The drug should be continued, — 8 to 10 grs doses — thrice daily for about ten days or a fortnight after the temperature is normal.

(VIII) After the salicylate is stopped,

111.

tonics, such as iron & quinine, should be given.

(IX) Stimulants may be given, but are rarely required.

(X) Hyperpnea is not affected by salicyl treatment.

(XI) Gonorrheal rheumatism, which is a distinct disease really from acute articular rheumatism, is not benefited by salicylates.

(XII) Pericarditis, endocarditis and myocarditis are not benefited by salicylates, and, in fact, the salicyl salts are often distinctly injurious in the last-named affection. The alkaloid, being more of a tonic than the acid or its salts, may possibly be used with some advantage, but even then is distinctly inferior to quinine.

(XIII) On the appearance of pleurisy,

pneumonia, or meningitis the
salicyl treatment should be
stopped.

— " —

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Added to this list must come the report, on Acute Rheumatism, by the Collective Investigation Committee of the British Medical Association, published in the Journal in Feb.^y 1888.^a

Influence of treatment on the duration of the rheumatic attack:-

| (Drug) | (Fever) | (Pain) | (Whole attack) |
|----------------------------|---------------------------------|----------------------------------|----------------------------------|
| Salicylates (Soc. & Pöts.) | 173 Cases. 86.5 d ^{ys} | 171 Cases. 10.18 d ^{ys} | 167 Cases. 19.03 d ^{ys} |
| Salicylic acid. | 9 " 13.8 " | 9 " 10.7 " | 9 " 10.7 " |
| Salicin. | 14 " 9.28 " | 14 " 15.07 " | 14 " 23.92 " |
| Alkalies. | 26 " 13.23 " | 26 " 19. " | 26 " 36.3 " |

FC

a. From the fact that the contents of this publication are so complete and exhaustive I have not tabulated the results of my references given; though, as far as the data in the latter are recorded, the outcome is very similar, but lacking in detail. So I have preferred to give a summary of the results of the investigation of the committee than create statistics

Fever seems to have been checked soonest (6.14 days) when the disease was treated by salicylates and blisters.

Pain subsided soonest (8.45 days) under treatment by salicylates and opium.

The whole attack seems to have been shortest (10.7 days) under the salicylic acid treatment.

By the different methods of treatment employed, the duration of the

| | | | | | |
|-------------------------|-------------|------|----|------|-----------|
| <u>fever</u> | varies from | 6.14 | to | 13.8 | days; |
| <u>pain</u> | " | " | " | 8.45 | " 24.16 " |
| <u>the whole attack</u> | " | 10.7 | " | 36.3 | " |

for myself out of the too often very imperfect results published in the medical journals. A.S.

Outward symptoms are noticed in the report as resulting from the employment of Salicin, Salicylic acid and its salts in 14 cases out of 536, or = 2.59 Pr. Ct. (5 of these were in cases treated by Salicin).

The symptoms were;—

| | | |
|---|--------------|--|
| 2 | instances of | Deafness & Delirium; |
| 2 | " " | Tinnitus; |
| 2 | " " | Delirium; |
| 1 | instance " | Nervous disturbance; |
| 1 | " " | Vomiting, diarrhoea & headache; |
| 1 | " " | Delirium, Dicrotic pulse & blackish urine; |
| 1 | " " | Gastro-enteritis & hæmaturia. |

Pericarditis occurred alone in 54 cases, or = 8.24 Pr. Ct., and, synchronously with endocarditis,

in 57 cases, or = 8.7 P. Ct.

Complications most frequently noted were; —

Pneumonia (in 1.52 P. Ct.),

Pleurisy (in 1.98 "),

Epistaxis (in 1.06 ").

Hyperpyrexia is reported

(the temperature exceeding at any one time 107° F.) in 4 of the total number of cases, with one recovery and 3 deaths.

Relapsing cases form 10.68 P. Ct. of the total number recorded.

Some had one relapse only; but, in 8 cases the relapses are stated to have been many.

Nearly twice as many males as females suffered from relapses,

and, throughout, it is seen that the more severe complications are generally much more frequent in males than among females.

Deaths occurred in 22 out of the 665 cases, or = 3.3 P.C.

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